STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 202218

TO: Rei-Tsang Shiao **Location: REM-5A10/5C18** **Art Unit: 1626** **Friday, September 22, 2006** **Case Serial Number: 10/821621**	**From: Paul Schulwitz** **Location: Biotech-Chem Library** **REM-1A65** **Phone: 571-272-2527** **Paul.schulwitz@uspto.gov**

Search Notes

Examiner Shiao,

Please review the attached search results.
If you have any questions or if you would like to refine the search query, please feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
REM-1A65
571-272-2527

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.

9-941

FOR OFFICIAL USE ONLY 202218 ACCESS DB # _____

PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Rebsang) Shiau Examiner #: 7954 Date: 9/18/06

Art Unit: 1626 Phone Number: 0707 Serial Number: 10/821,621

Location (Bldg/Room#): REM (Mailbox #): 5A19 / 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Simple stereochem

Inventors (please provide full names): Corey

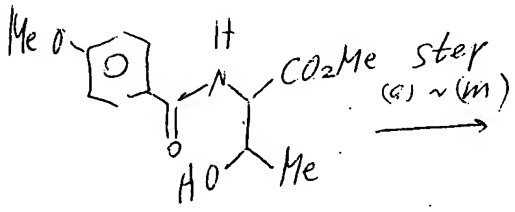
Earliest Priority Date: _____

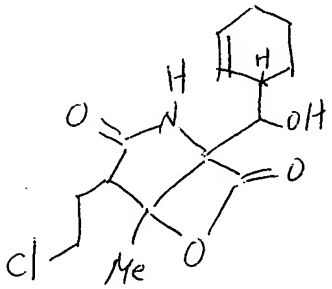
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

I. such a process of making cpd 2 by:





cpd I

CA

L31

L32

L33

BS

L55

INV

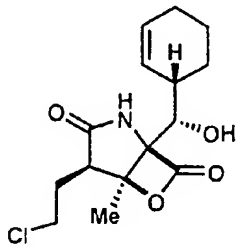
L42

IN THE CLAIMS:

Please amend the claims as shown in the following Claim Listing.

CLAIM LISTING:

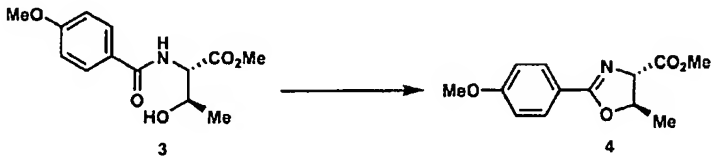
1. (Original) A process for the enantiospecific total synthesis of the compound of structure 1:



1

comprising the steps of:

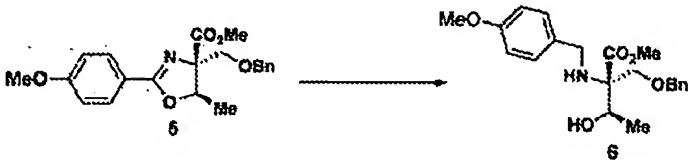
(a) converting amide 3 to oxazoline 4:



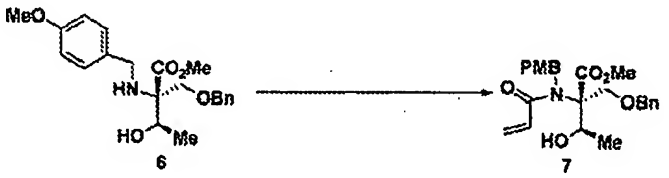
3 4

(b) deprotonating 4 followed by alkylation of the resulting enolate to provide 5:

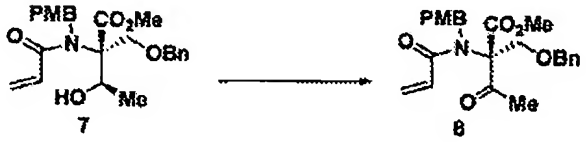
(c) reducing 5 to yield the N-4-methoxybenzylamine 6:



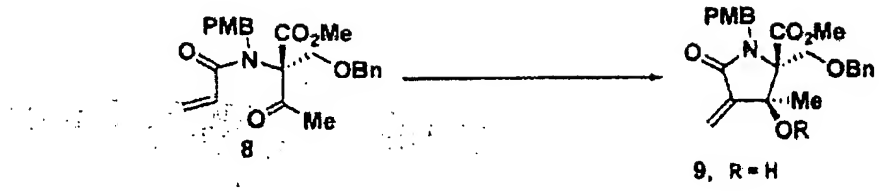
(d) acylating 6a (structure not shown, OH in 6 is OTMS) to afford the N-acrylyl-N-PMB derivative 7:



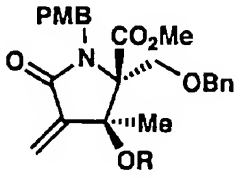
(e) oxidizing 7 to produce the keto amide ester 8:



(f) cyclizing 8 to afford the γ-lactam 9:

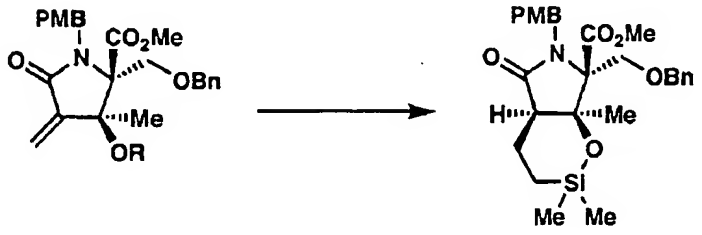


(g) silylating 9 to produce the silyl ether 11:



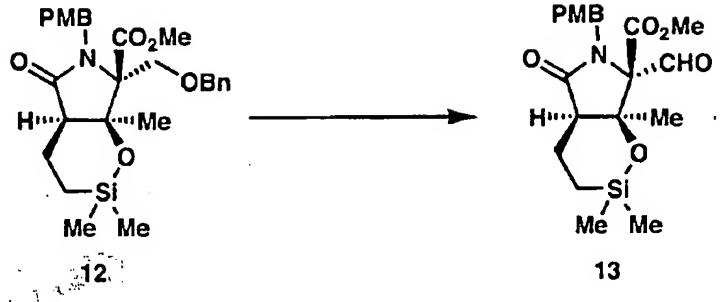
9, R = H
11, R = $Si(Me)_2CH_2Br$

(h) cyclizing 11 to provide the *cis*-fused γ-lactam 12:

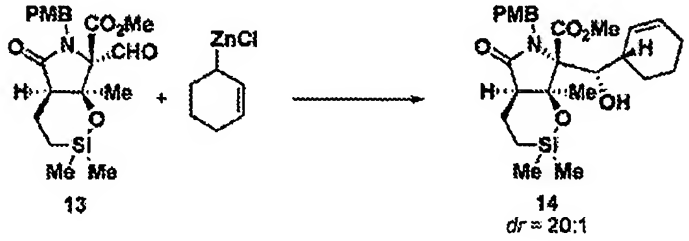


11 12

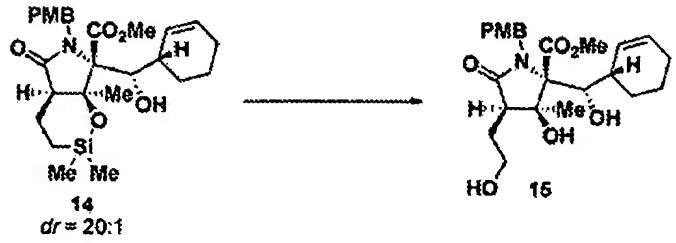
(i) cleaving the protecting group (OBn) in compound 12 to yield the primary alcohol 12a (wherein OBn in 12 is OH), and oxidizing 12a to provide the aldehyde 13:



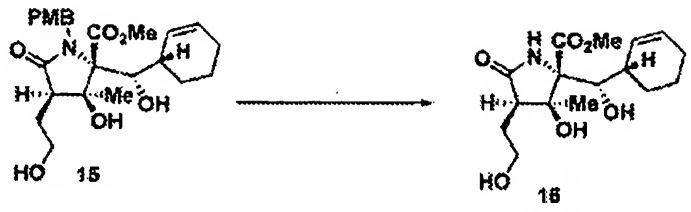
(j) reacting 2-cyclo-hexenylzinc chloride with the aldehyde 13 to yield the formyl adduct 14:



(k) oxidizing 14 to provide the triol 15:

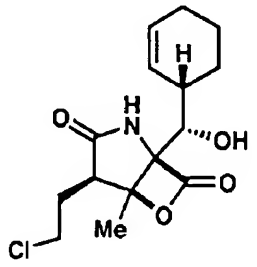


(l) cleaving the PMB group of 15 to yield the triol ester 16:



(m) hydrolyzing 16 to the corresponding γ-lactam-carboxylic acid 16a (CO_2Me in 16 is CO_2H), followed by conversion of the acid 16a to the beta-lactone 16b, followed by conversion to salinosporamide A (1):

16 → 16a → 16b →



1

2. (Original) The intermediate step (b) of Claim 1, namely the deprotonation of 4 followed by alkylation of the resulting enolate to provide 5:

4 5

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Bib Data Sheet

CONFIRMATION NO. 8936

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/821,621	04/09/2004 RULE	548	1626	004979-00045

APPLICANTS

Elias J. Corey, Cambridge, MA;

** CONTINUING DATA **********

** FOREIGN APPLICATIONS **********

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 06/26/2004

		STATE OR	SHEETS	TOTAL	INDEPENDENT
Foreign Priority claimed	☐ yes ☒ no	COUNTRY	DRAWING	CLAIMS	CLAIMS
35 USC 119 (a-d) conditions met	☑ yes ☐ no ☐ Met after Allowance	MA	1	27	1
Verified and Acknowledged	Examiner's Signature Initials				

ADDRESS
22910
BANNER & WITCOFF, LTD.
28 STATE STREET
28th FLOOR
BOSTON , MA
02109-9601

TITLE
Simple stereocontrolled synthesis of salinosporamide A

FILING FEE	FEES: Authority has been given in Paper	☐ All Fees
RECEIVED 1026	No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____

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-> d his nofil

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L13 4 SEA ABB=ON PLU=ON L12 AND C6/ES AND O>4 AND NR=1 AND N>0
D SCA

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L14 7 SEA ABB=ON PLU=ON L13(L)RACT+NT/RL

FILE 'REGISTRY' ENTERED AT 10:07:47 ON 22 SEP 2006

L15 9 SEA ABB=ON PLU=ON L12 AND (C6 AND NCOC2)/ES AND O>3

FILE 'HCAPLUS' ENTERED AT 10:08:18 ON 22 SEP 2006

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L17 123 SEA ABB=ON PLU=ON C6/ES AND O>4 AND L12

FILE 'HCAPLUS' ENTERED AT 10:09:18 ON 22 SEP 2006

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L19 144 SEA ABB=ON PLU=ON O>4 AND N>0 AND L12

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L21 1262292 SEA ABB=ON PLU=ON SI/ELS

FILE 'HCAPLUS' ENTERED AT 10:10:55 ON 22 SEP 2006

FILE 'REGISTRY' ENTERED AT 10:11:02 ON 22 SEP 2006

L22 30 SEA ABB=ON PLU=ON SI/ELS AND L12

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D SCA

FILE 'HCAPLUS' ENTERED AT 10:11:58 ON 22 SEP 2006

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L27 1537291 SEA ABB=ON PLU=ON NC4/ES

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L31            8 SEA ABB=ON  PLU=ON  L30 AND L11
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L*** DEL      16 S L31 OR L32 OR L33
L*** DEL       1 S L1 AND L31

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L40           15 SEA ABB=ON  PLU=ON  L38 AND ?SPORAMID?
L41           16 SEA ABB=ON  PLU=ON  L39 OR L40
L42            7 DUP REM L41 (9 DUPLICATES REMOVED)
                       ANSWERS '1-7' FROM FILE HCAPLUS

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                 D QUE L31

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L3             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L2
```

INSTANT APPLICATION

```
=> d l3 iall hitstr

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1106831  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:386848
ENTRY DATE:               Entered STN:  14 Oct 2005
TITLE:                    Simple stereocontrolled synthesis of salinosporamide A
INVENTOR(S):              Corey, Elias J.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 17 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
INT. PATENT CLASSIF.:
            MAIN:         C07D491-02
US PATENT CLASSIF.:       548453000
CLASSIFICATION:           26-6 (Biomolecules and Their Synthetic Analogs)
                          Section cross-reference(s): 34
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     --------------       ----   --------    --------------------    --------
     US 2005228186         A1    20051013    US 2004-821621          20040409 <--
     WO 2005113558         A2    20051201    WO 2005-US12218         20050411 <--
     WO 2005113558         A3    20051222
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
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             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 2004-821621      A  20040409 <--
PATENT CLASSIFICATION CODES:
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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	INCL	548453000
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	IPCR	C07D0491-00 [I,C*]; C07D0491-02 [I,A]
	NCL	548/453.000
	ECLA	C07D207/38; C07D263/16B; C07D491/04+305B+209B
WO 2005113558	IPCI	C07D0491-02 [ICM,7]; C07D0491-00 [ICM,7,C*]
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OTHER SOURCE(S): CASREACT 143:386848

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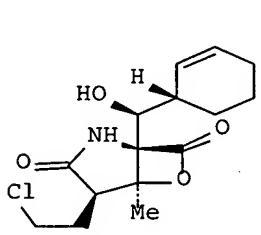

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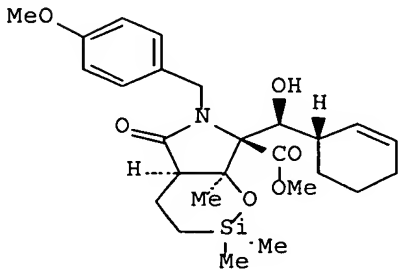


II

ABSTRACT:
A simple and effective stereocontrolled synthesis of (-)-salinosporamide A (I) was disclosed. The process, the first total synthesis of salinosporamide A, is capable of providing the compound in substantial quantities for further biol. studies. The disclosed synthetic scheme started from N-(4-methoxybenzoyl)-L-threonine Me ester and included the preparation of several novel synthetic intermediate compds., such as lactam II. Salinosporamide A is a synthetic target of special interest because it has previously shown proteasome inhibiting activity and shown cytotoxic activity in vitro against many tumor cell lines (IC50 values of 10 nM or less).

SUPPL. TERM: salinosporamide A asym synthesis

INDEX TERM: Asymmetric synthesis and induction
(asym. synthesis of salinosporamide A)

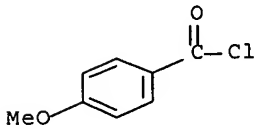
INDEX TERM: **100-07-2**, 4-Methoxybenzoyl chloride **814-68-6**, Acryloyl chloride **3373-59-9**, L-Threonine methyl ester **3587-60-8 16532-02-8**, (Bromomethyl)chlorodimethylsilane **112520-99-7**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(asym. synthesis of salinosporamide A)

INDEX TERM: **704910-28-1P**, N-(4-Methoxybenzoyl)-L-threonine methyl ester **704910-29-2P 704910-30-5P 704910-31-6P 704910-32-7P 704910-33-8P 704910-34-9P 704910-35-0P 704910-36-1P 704910-37-2P 704910-38-3P 704910-39-4P 704910-41-8P 704910-42-9P 704910-44-1P 704910-45-2P**
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of salinosporamide A)

INDEX TERM: 437742-34-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of salinosporamide A)

IT 100-07-2, 4-Methoxybenzoyl chloride 814-68-6, Acryloyl chloride 3373-59-9, L-Threonine methyl ester 3587-60-8 16532-02-8, (Bromomethyl)chlorodimethylsilane 112520-99-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. synthesis of salinosporamide A)

RN 100-07-2 HCAPLUS
CN Benzoyl chloride, 4-methoxy- (9CI) (CA INDEX NAME)



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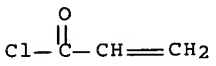
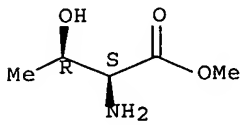
CN 2-Propenoyl chloride (9CI) (CA INDEX NAME)

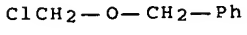


RN 3373-59-9 HCAPLUS
CN L-Threonine, methyl ester (9CI) (CA INDEX NAME)

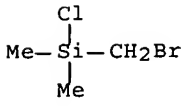
Absolute stereochemistry. Rotation (-).



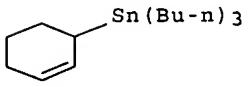
RN 3587-60-8 HCAPLUS
CN Benzene, [(chloromethoxy)methyl]- (9CI) (CA INDEX NAME)



RN 16532-02-8 HCAPLUS
CN Silane, (bromomethyl)chlorodimethyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 112520-99-7 HCAPLUS
CN Stannane, tributyl-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



IT 704910-28-1P, N-(4-Methoxybenzoyl)-L-threonine methyl ester
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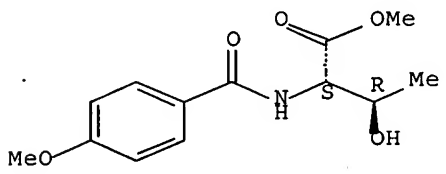
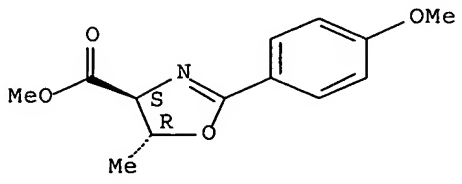
704910-32-7P 704910-33-8P 704910-34-9P
704910-35-0P 704910-36-1P 704910-37-2P
704910-38-3P 704910-39-4P 704910-41-8P
704910-42-9P 704910-44-1P 704910-45-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of salinosporamide A)
RN 704910-28-1 HCAPLUS
CN L-Threonine, N-(4-methoxybenzoyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



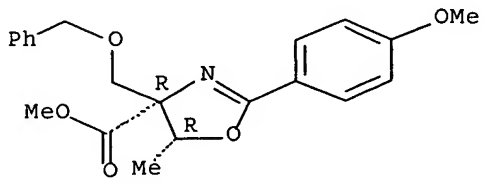
RN 704910-29-2 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



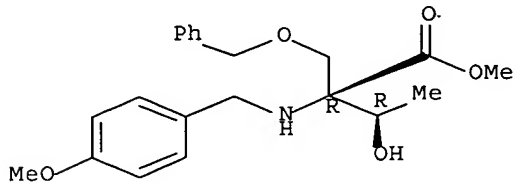
RN 704910-30-5 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-4-[(phenylmethoxy)methyl]-, methyl ester, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



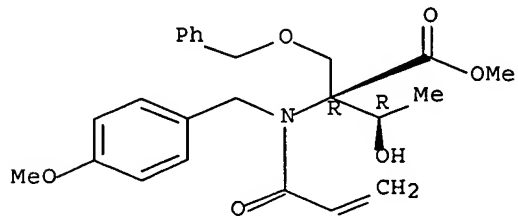
RN 704910-31-6 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



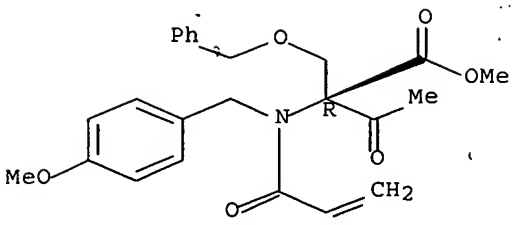
RN 704910-32-7 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



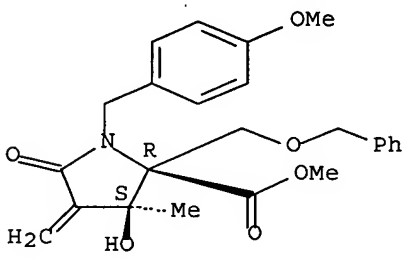
RN 704910-33-8 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



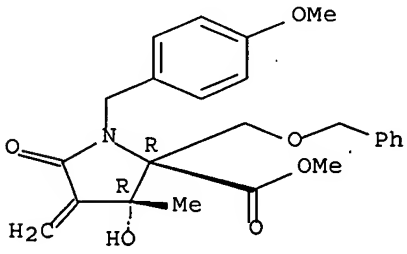
RN 704910-34-9 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



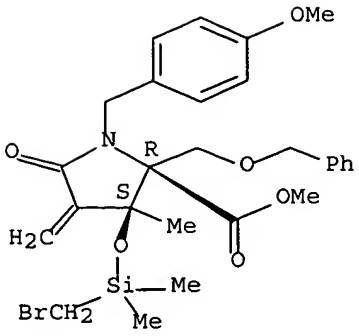
RN 704910-35-0 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



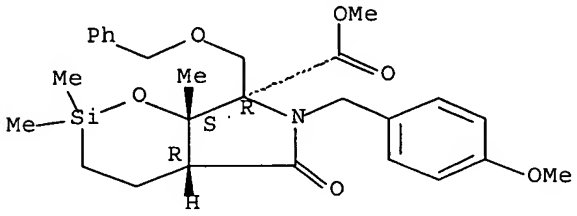
RN 704910-36-1 HCAPLUS
CN D-Proline, 3-[[(bromomethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



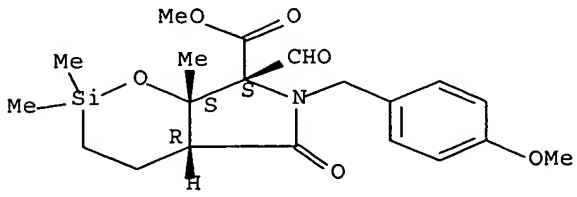
RN 704910-37-2 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-7-[(phenylmethoxy)methyl]-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



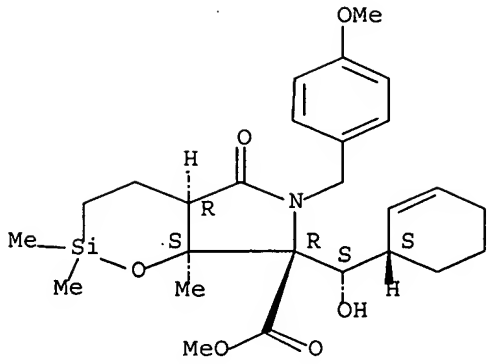
RN 704910-38-3 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-formyloctahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7S,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



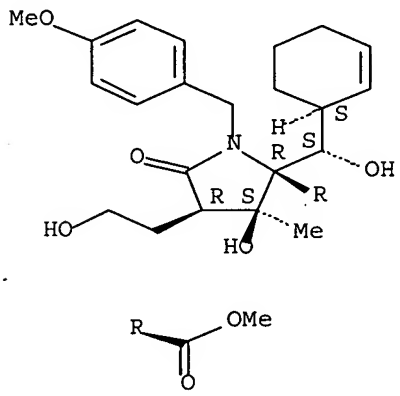
RN 704910-39-4 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



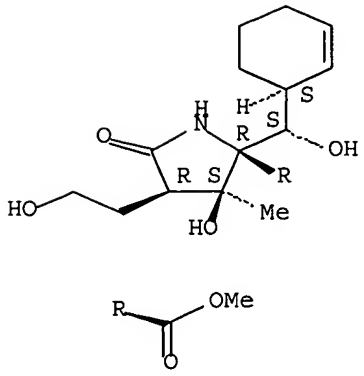
RN 704910-41-8 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



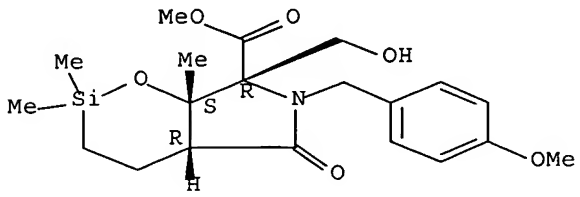
RN 704910-42-9 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 704910-44-1 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-(hydroxymethyl)-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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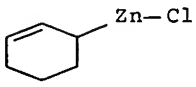
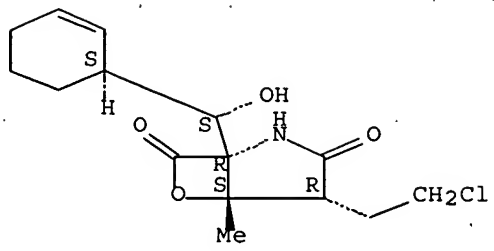
CN Zinc, chloro-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



IT **437742-34-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of salinosporamide A)
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).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PRIOR ART SEARCH

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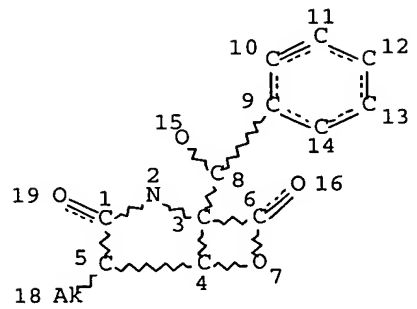

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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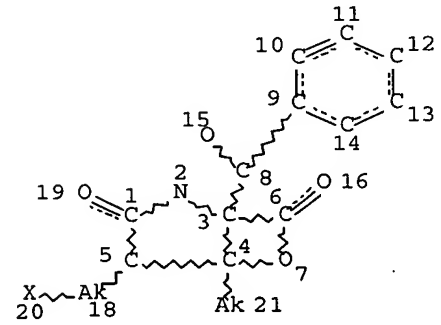
L7 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)PREP+NT/RL
L8 STR



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NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
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L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND C6/ES AND O>4 AND NR=1 AND N>0
L14 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L13(L)RACT+NT/RL
L15 9 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND (C6 AND NCOC2)/ES AND O>3
L16 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L15(L)RACT+NT/RL AND L15(L)PREP+NT/RL
L17 123 SEA FILE=REGISTRY ABB=ON PLU=ON C6/ES AND O>4 AND L12
L18 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L17(L)RACT+NT/RL AND L17(L)PREP+NT/RL
L19 144 SEA FILE=REGISTRY ABB=ON PLU=ON O>4 AND N>0 AND L12
L20 119 SEA FILE=HCAPLUS ABB=ON PLU=ON L19(L)RACT+NT/RL AND L19(L)PREP+NT/RL
L22 30 SEA FILE=REGISTRY ABB=ON PLU=ON SI/ELS AND L12
L23 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L)RACT+NT/RL AND L22(L)PREP+NT/RL
L24 1 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND ZN/ELS
L25 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L24(L)RACT+NT/RL
L27 1537291 SEA FILE=REGISTRY ABB=ON PLU=ON NC4/ES
L28 69 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND L27
L29 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L28(L)RACT+NT/RL AND L28(L)PREP+NT/RL
L30 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND (L14 OR L16 OR L18 OR L20 OR L23 OR L25 OR L29)
L31 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L11

=> d l31 ibib abs hitstr 1-8

L31 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:544606 HCAPLUS Full-text
DOCUMENT NUMBER: 145:45846

TITLE: Preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compositions

INVENTOR(S): Palladino, Michael; Potts, Barbara Christine; Macherla, Venkata Rami Reddy; Neuteboom, Saskia Theodora Cornelia

PATENT ASSIGNEE(S): Nereus Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060809	A2	20060608	WO 2005-US44091	20051202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

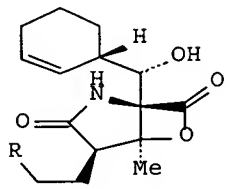
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2004-633379P	P	20041203
US 2005-643922P	P	20050113
US 2005-658884P	P	20050304
US 2005-676533P	P	20050429

OTHER SOURCE(S): MARPAT 145:45846

GI



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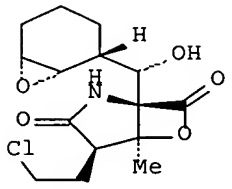


II

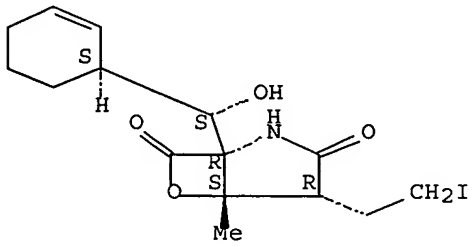
AB Salinosporamide A I (R = Cl) and its analogs were prepared for therapeutic use in the treatment of cancer, inflammatory conditions, and/or infectious disease. I was prepared via a fermentation process using strain CNB476 or strain NPS21184. I and related bicyclic β-lactones recovered from the fermentation process were subsequently converted to other β-lactone derivs., such as I (R = H, Br, iodo, Me) and II. The prepared β-lactones were extensively tested for anticancer, anti-inflammatory and antibacterial activity.

IT **823229-34-1P 823229-42-1P 872360-17-3P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); **RCT (Reactant)**; **SPN (Synthetic preparation)**

; THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compns.)

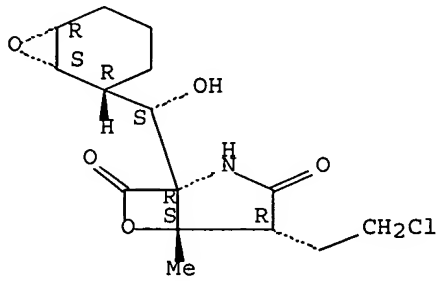
RN 823229-34-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-iodoethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



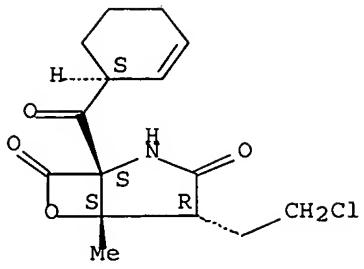
RN 823229-42-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1S,2R,6R)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 872360-17-3 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(1S)-2-cyclohexen-1-ylcarbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

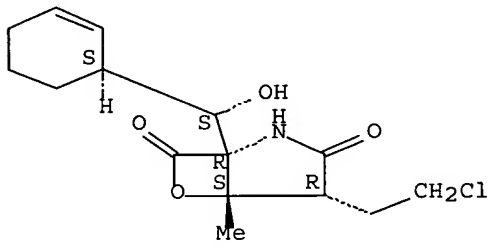
Absolute stereochemistry.



IT **437742-34-2P**, Salinosporamide A **863126-95-8P**
872360-15-1P
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compns.)

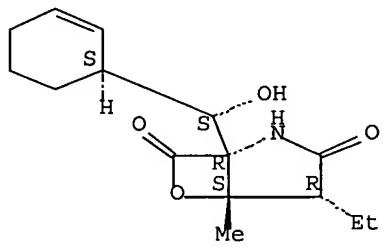
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 863126-95-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

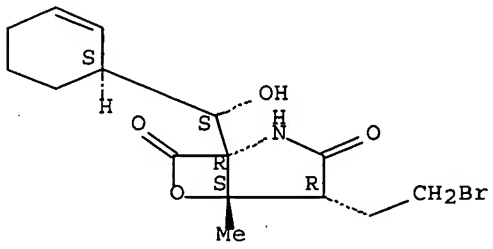
Absolute stereochemistry. Rotation (-).



RN 872360-15-1 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-bromoethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

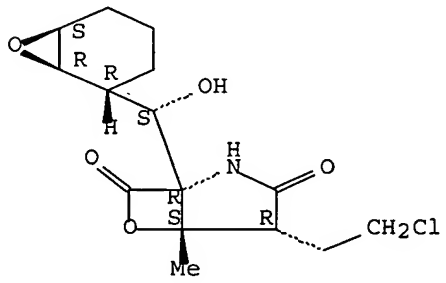


IT **823229-44-3P 823229-46-5P 823229-54-5P**
823229-56-7P 872360-18-4P 872360-19-5P
872360-20-8P 872360-21-9P 872360-22-0P
872360-23-1P 872360-24-2P 872360-25-3P
872360-26-4P 872360-27-5P 872360-28-6P
872360-29-7P 872360-30-0P 872360-31-1P
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compns.)

RN 823229-44-3 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1R,2R,6S)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

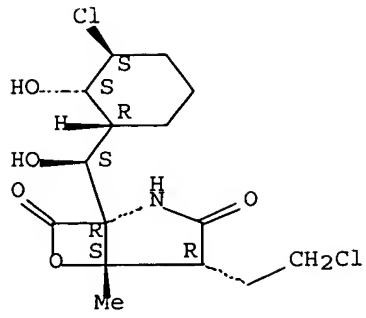
Absolute stereochemistry.



RN 823229-46-5 HCAPLUS

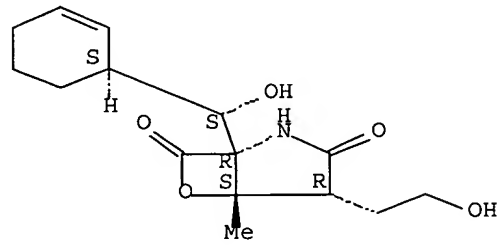
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1R,2S,3S)-3-chloro-2-hydroxycyclohexyl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



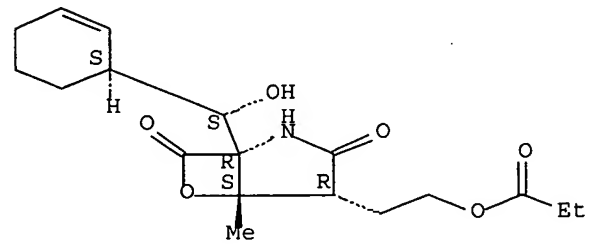
RN 823229-54-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-hydroxyethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



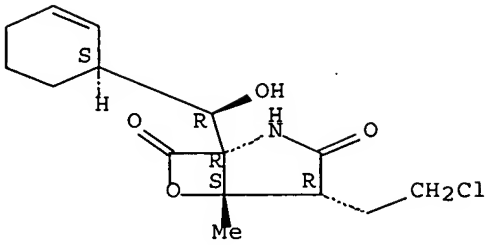
RN 823229-56-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-4-[2-(1-oxopropoxy)ethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



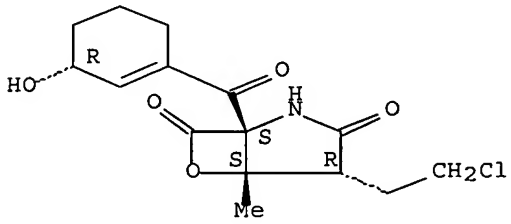
RN 872360-18-4 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(R)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



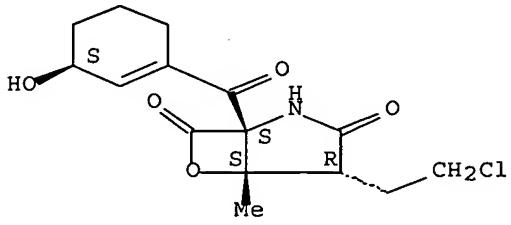
RN 872360-19-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[[(3R)-3-hydroxy-1-cyclohexen-1-yl]carbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



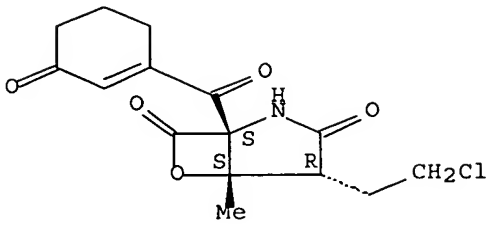
RN 872360-20-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[[(3S)-3-hydroxy-1-cyclohexen-1-yl]carbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



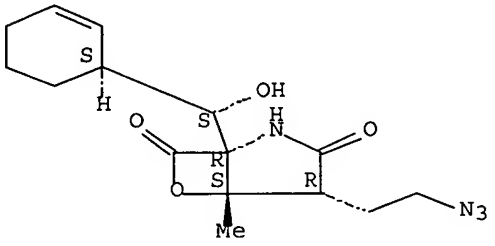
RN 872360-21-9 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-5-methyl-1-[(3-oxo-1-cyclohexen-1-yl)carbonyl]-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



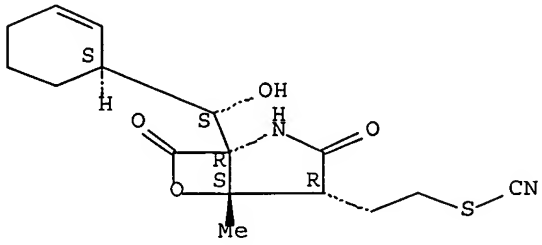
RN 872360-22-0 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-azidoethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



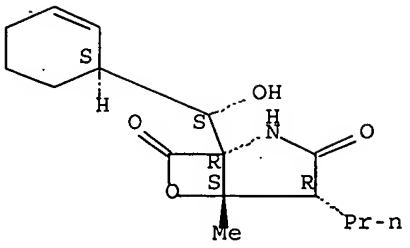
RN 872360-23-1 HCAPLUS
CN Thiocyanic acid, 2-[(1R,4R,5S)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-3,7-dioxo-6-oxa-2-azabicyclo[3.2.0]hept-4-yl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



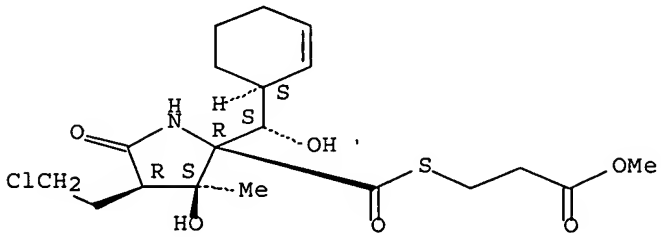
RN 872360-24-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-4-propyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



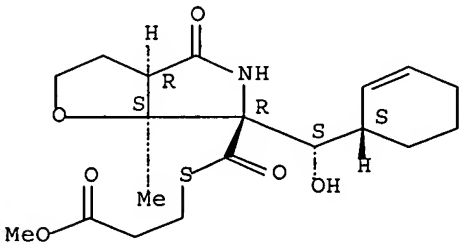
RN 872360-25-3 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



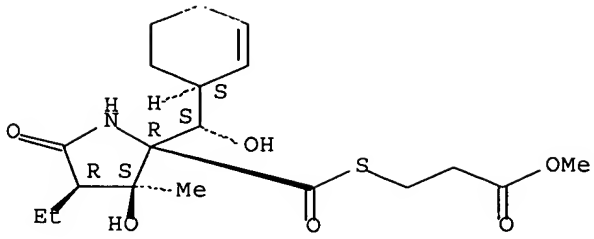
RN 872360-26-4 HCAPLUS
CN Propanoic acid, 3-[[[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrol-6-yl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 872360-27-5 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

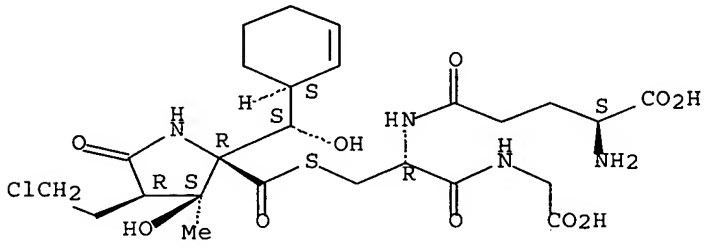
Absolute stereochemistry.



RN 872360-28-6 HCAPLUS

CN Glycine, L-γ-glutamyl-S-[(3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-D-prolyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

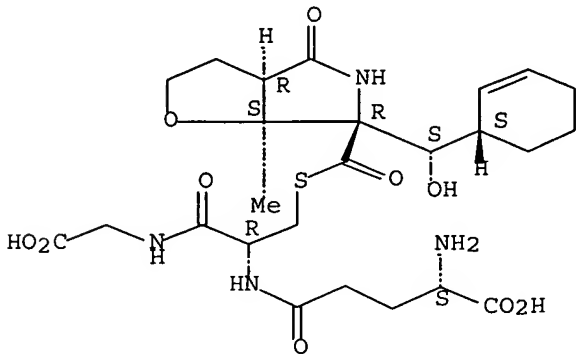
Absolute stereochemistry.



RN 872360-29-7 HCAPLUS

CN Glycine, L-γ-glutamyl-S-[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrole-6-carbonyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

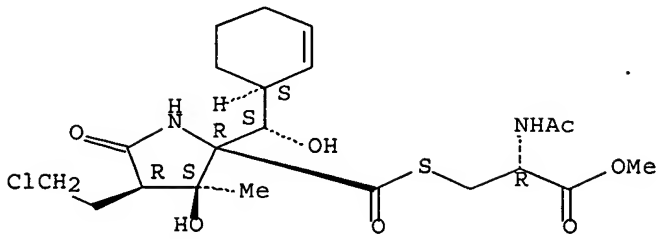
Absolute stereochemistry.



RN 872360-30-0 HCAPLUS

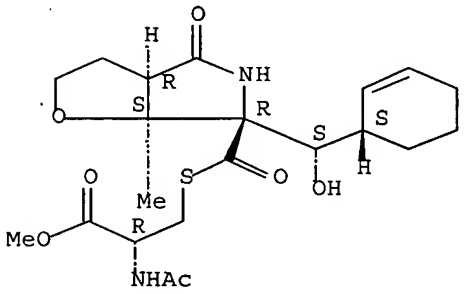
CN L-Cysteine, N-acetyl-S-[(3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-D-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



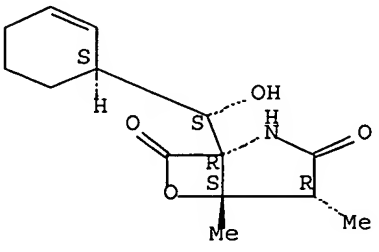
RN 872360-31-1 HCAPLUS
CN L-Cysteine, N-acetyl-S-[[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrol-6-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



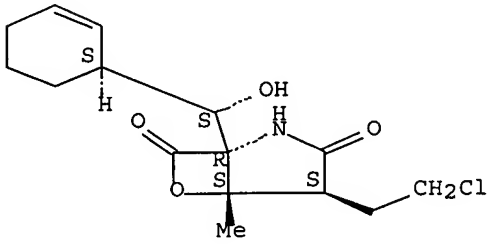
IT **823229-26-1P 872360-11-7P 872360-12-8P**
872360-13-9P 872360-16-2P
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compns.)
RN 823229-26-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-dimethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



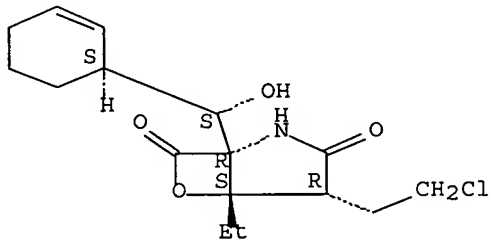
RN 872360-11-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



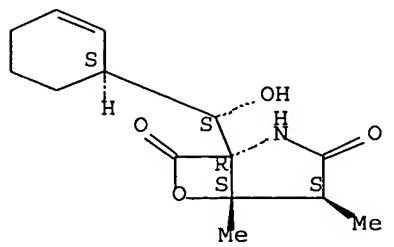
RN 872360-12-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-ethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



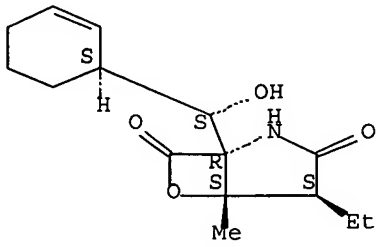
RN 872360-13-9 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-dimethyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



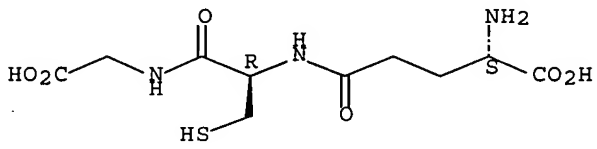
RN 872360-16-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-5-methyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 70-18-8, Glutathione, reactions
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation of salinosporamide A and analogous [3.2.0] bicyclic β-lactones for use in anti-cancer pharmaceutical compns.)
RN 70-18-8 HCAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



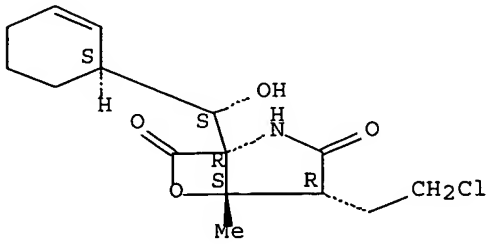
L31 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:529516 HCAPLUS Full-text
DOCUMENT NUMBER: 145:188596
TITLE: Studies toward the synthesis of salinosporamide A, a potent proteasome inhibitor
AUTHOR(S): Caubert, Virginie; Langlois, Nicole
CORPORATE SOURCE: Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, 91198, Fr.
SOURCE: Tetrahedron Letters (2006), 47(26), 4473-4475
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An α-methylenepyrrolidinone bearing all the functionalities and relative configurations of an advanced intermediate in the synthesis of salinosporamide A and analogs was synthesized from Me pyroglutamate through regio- and stereoselective N-methylnitrone cycloaddn.

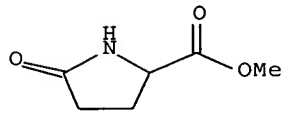
IT 437742-34-2P, Salinosporamide A
RL: **PNU (Preparation, unclassified); PREP (Preparation)**
(preparation of methylenepyrrolidinone as salinosporamide A precursor from pyroglutamate by regio- and stereoselective nitrone cycloaddn.)

RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

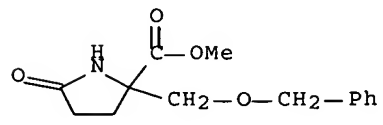
Absolute stereochemistry. Rotation (-).



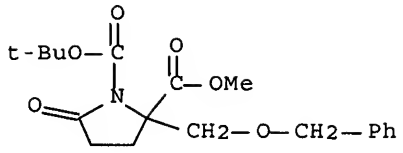
IT 54571-66-3, DL-Methyl pyroglutamate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methylenepyrrolidinone as salinosporamide A precursor from pyroglutamate by regio- and stereoselective nitrone cycloaddn.)
RN 54571-66-3 HCAPLUS
CN Proline, 5-oxo-, methyl ester (9CI) (CA INDEX NAME)



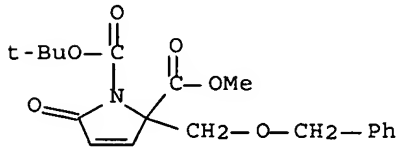
IT 903528-00-7P 903528-01-8P 903528-02-9P
903528-03-0P 903528-04-1P 903528-05-2P
903528-06-3P 903528-08-5P 903528-09-6P
903528-11-0P
RL: RCT (Reactant); SPN (Synthetic preparation);
PREP (Preparation); RACT (Reactant or reagent)
(preparation of methylenepyrrolidinone as salinosporamide A precursor from pyroglutamate by regio- and stereoselective nitrone cycloaddn.)
RN 903528-00-7 HCAPLUS
CN Proline, 5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)



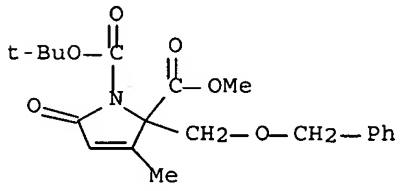
RN 903528-01-8 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 903528-02-9 HCAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 2,5-dihydro-5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)

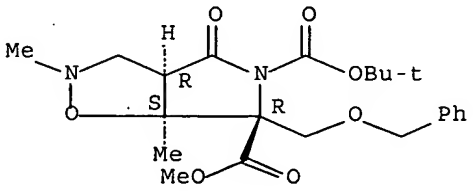


RN 903528-03-0 HCAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 2,5-dihydro-3-methyl-5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 903528-04-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

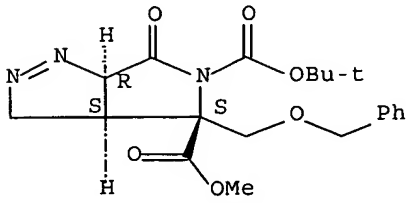
Relative stereochemistry.



RN 903528-05-2 HCAPLUS

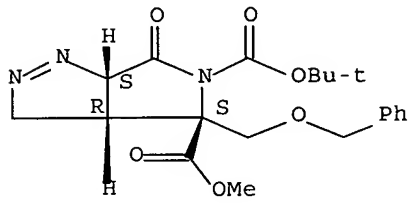
CN Pyrrolo[3,4-c]pyrazole-4,5(3H)-dicarboxylic acid, 3a,4,6,6a-tetrahydro-6-oxo-4-[(phenylmethoxy)methyl]-, 5-(1,1-dimethylethyl) 4-methyl ester, (3aR,4R,6aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



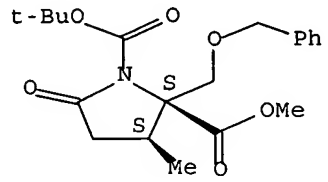
RN 903528-06-3 HCAPLUS
CN Pyrrolo[3,4-c]pyrazole-4,5(3H)-dicarboxylic acid, 3a,4,6,6a-tetrahydro-6-oxo-4-[(phenylmethoxy)methyl]-, 5-(1,1-dimethylethyl) 4-methyl ester, (3aR,4S,6aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



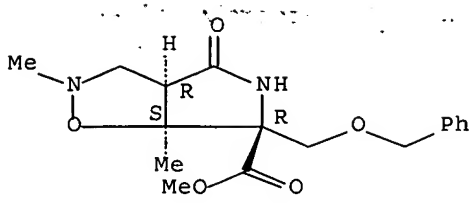
RN 903528-08-5 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-methyl-5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



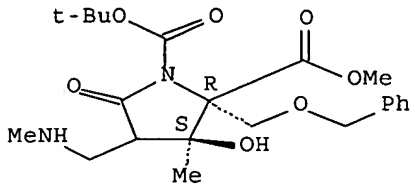
RN 903528-09-6 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



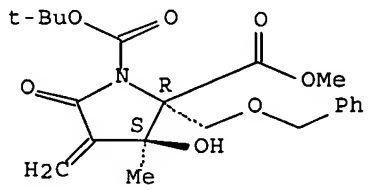
RN 903528-11-0 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-hydroxy-3-methyl-4-[(methylamino)methyl]-5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2R,3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

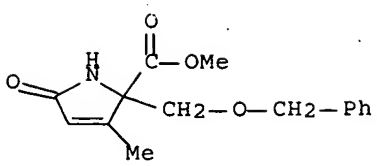


IT **903527-99-1P 903528-07-4P 903528-10-9P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of methylenepyrrolidinone as salinosporamide A precursor from pyroglutamate by regio- and stereoselective nitrone cycloaddn.)
RN 903527-99-1 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-hydroxy-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2R,3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

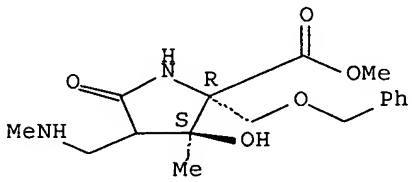


RN 903528-07-4 HCAPLUS
CN 1H-Pyrrole-2-carboxylic acid, 2,5-dihydro-3-methyl-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)



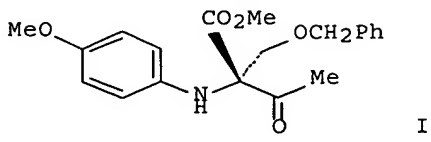
RN 903528-10-9 HCAPLUS
CN D-Proline, 3-hydroxy-3-methyl-4-[(methylamino)methyl]-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:274086 HCAPLUS Full-text
DOCUMENT NUMBER: 145:7903
TITLE: Novel Bicyclization Reaction Leading to a Fused β-Lactone
AUTHOR(S): Reddy, Leleti Rajender; Corey, E. J.
CORPORATE SOURCE: Harvard University, Cambridge, MA, 02138, USA
SOURCE: Organic Letters (2006), 8(8), 1717-1719
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The reaction of acryloyl chloride with the amino ketone I in the presence of pyridine produces bicyclic β-lactones rather than the corresponding acrylamide, which can be the major product under other conditions and which is an intermediate for the synthesis of salinosporamide A.
IT **704910-33-8P**

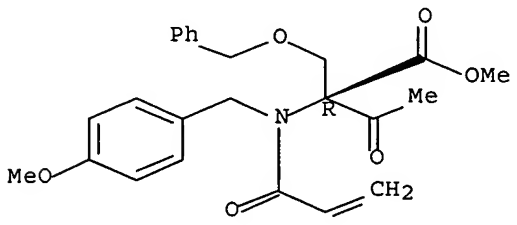
RL: **BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)**

(novel bicyclization reaction leading to a fused β-lactone)

RN 704910-33-8 HCAPLUS

CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **437742-34-2P**, Salinosporamide A

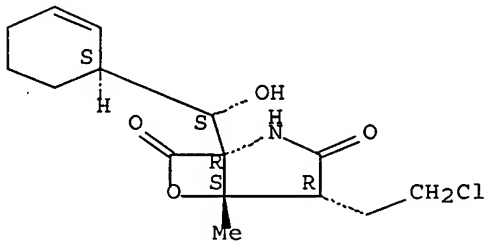
RL: **PNU (Preparation, unclassified); PREP (Preparation)**

(novel bicyclization reaction leading to a fused β-lactone)

RN 437742-34-2 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **887776-08-1P**

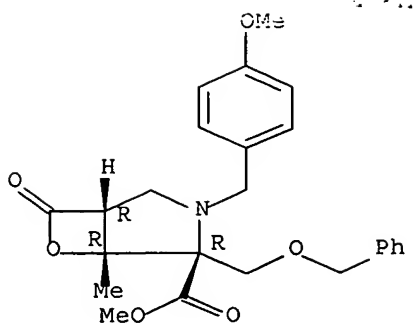
RL: PRP (Properties); **SPN (Synthetic preparation); PREP (Preparation)**

(novel bicyclization reaction leading to a fused β-lactone)

RN 887776-08-1 HCAPLUS

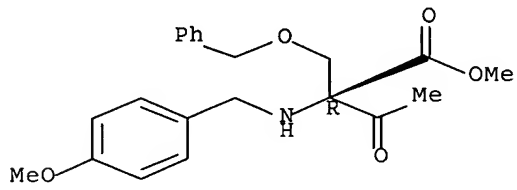
CN 6-Oxa-3-azabicyclo[3.2.0]heptane-4-carboxylic acid, 3-[(4-methoxyphenyl)methyl]-5-methyl-7-oxo-4-[(phenylmethoxy)methyl]-, methyl ester, (1R,4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



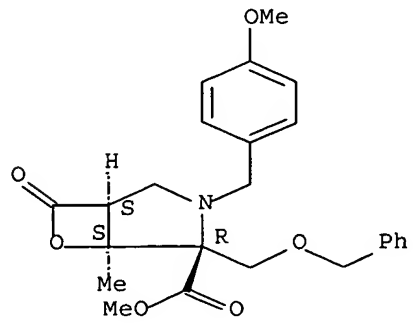
IT 887776-07-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel bicyclization reaction leading to a fused β-lactone)
RN 887776-07-0 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 887776-09-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel bicyclization reaction leading to a fused β-lactone)
RN 887776-09-2 HCAPLUS
CN 6-Oxa-3-azabicyclo[3.2.0]heptane-4-carboxylic acid, 3-[(4-methoxyphenyl)methyl]-5-methyl-7-oxo-4-[(phenylmethoxy)methyl]-, methyl ester, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1348855 HCAPLUS Full-text
DOCUMENT NUMBER: 144:81222
TITLE: Preparation of [3.2.0] heterocyclic compounds and treatment methods of using the same
INVENTOR(S): Potts, Barbara Christine; Macherla, Venkat; Mitchell, Scott Sherman; Manam, Ram Rao; Reed, Katherine; Lam, Kin Sing; Neuteboom, Saskia; Chao, Ta-Hsiang; Nicholson, Benjamin; Billstrom, Cheryl
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 94 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

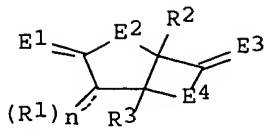
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005288352	A1	20051229	US 2005-118260	20050429
WO 2006028525	A2	20060316	WO 2005-US14846	20050429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2004-567336P	P	20040430
US 2004-580838P	P	20040618
US 2004-591190P	P	20040726
US 2004-627462P	P	20041112
US 2005-644132P	P	20050113
US 2005-659385P	P	20050304

OTHER SOURCE(S): MARPAT 144:81222
GI



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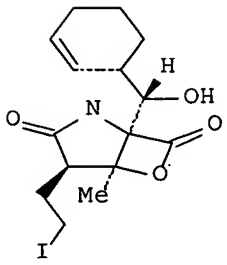

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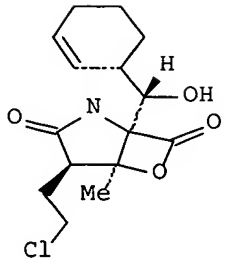


III

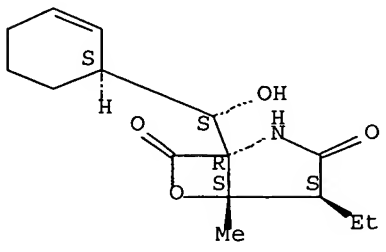
AB [3.2.0]-Bicycloheptanes I [R1 = H, halo, (un)substituted alkyl, etc.; R2 = H, halo, (un)substituted alkyl, alkenyl, etc.; R3 = halo, (un)substituted aryl, cycloalkyl, etc.; E1-4 independently = (un)substituted heteroatom; with provisions] and derivs. thereof, are prepared and disclosed as having anti-cancer, anti-inflammatory, and anti-microbial properties. Thus, e.g., II was prepared by iodination of fermentation product III. In assays of growth inhibition of human multiple myeloma, II for example demonstrated EC50 values (nM) of 5.9 and 3.2 resp. against RPMI 8226 and U266 cell lines. Pharmaceutical compns. comprising such compds. and methods of treating cancer, inflammatory conditions, and microbial infections with the disclosed compds. or the disclosed pharmaceutical compns. are also disclosed.

IT **872360-16-2P**
RL: **BPN (Biosynthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

RN 872360-16-2 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-5-methyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

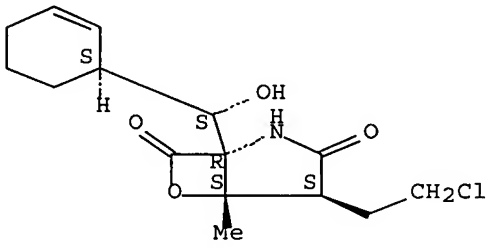


IT **872360-11-7P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological

activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

RN 872360-11-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

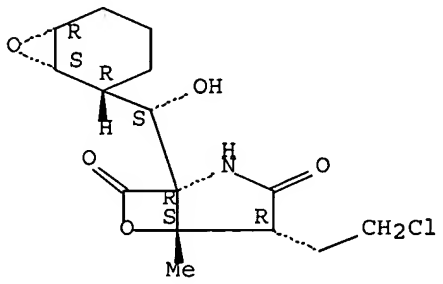
Absolute stereochemistry.



IT **823229-42-1P 872360-17-3P 872360-18-4P 872360-28-6P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); **RCT (Reactant)**; **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; **RACT (Reactant or reagent)**; USES (Uses)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

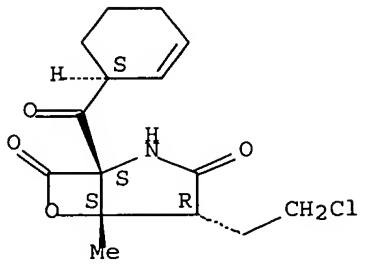
RN 823229-42-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1S,2R,6R)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



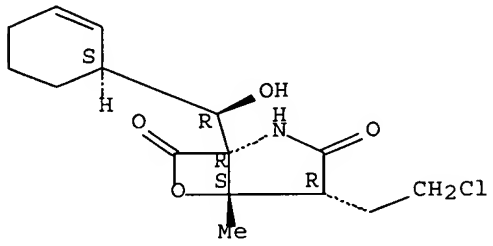
RN 872360-17-3 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(1S)-2-cyclohexen-1-ylcarbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry



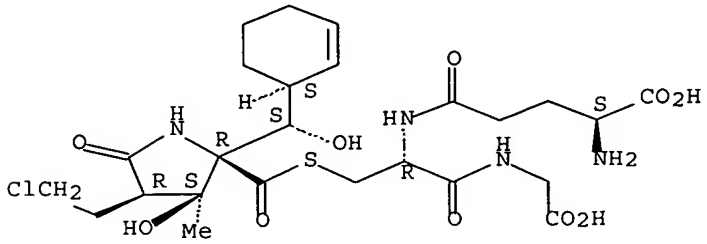
RN 872360-18-4 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(R)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 872360-28-6 HCAPLUS
CN Glycine, L-γ-glutamyl-S-[(3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-D-prolyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



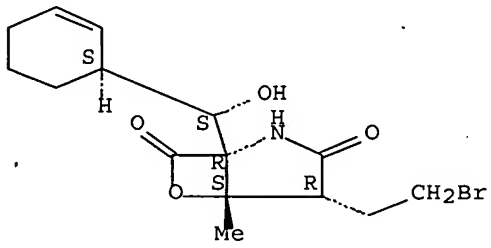
IT **872360-15-1P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation

process
for treatment of cancer, inflammatory conditions, and microbial infections)

RN 872360-15-1 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-bromoethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

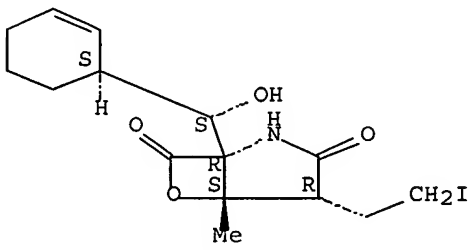


IT 823229-34-1P 823229-44-3P 823229-46-5P
823229-54-5P 823229-56-7P 872360-19-5P
872360-20-8P 872360-22-0P 872360-23-1P
872360-24-2P 872360-25-3P 872360-26-4P
872360-27-5P 872360-30-0P
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

RN 823229-34-1 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-iodoethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

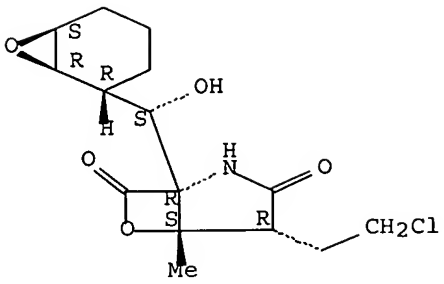
Absolute stereochemistry.



RN 823229-44-3 HCAPLUS

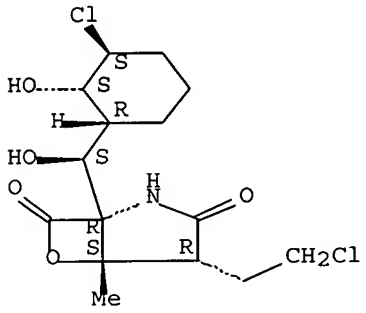
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1R,2R,6S)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



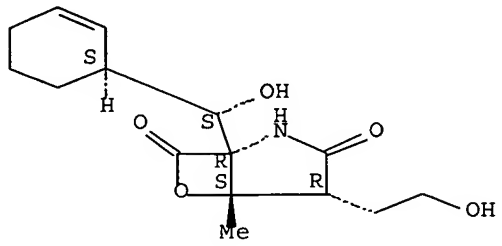
RN 823229-46-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1R,2S,3S)-3-chloro-2-hydroxycyclohexyl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



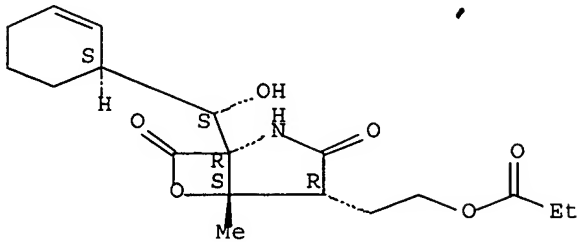
RN 823229-54-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-hydroxyethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



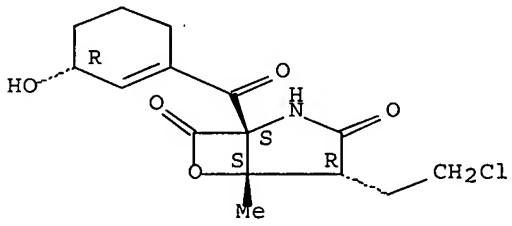
RN 823229-56-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-4-[2-(1-oxopropoxy)ethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



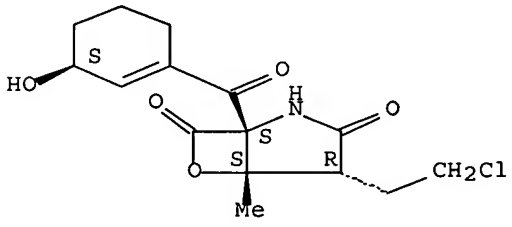
RN 872360-19-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[[(3R)-3-hydroxy-1-cyclohexen-1-yl]carbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



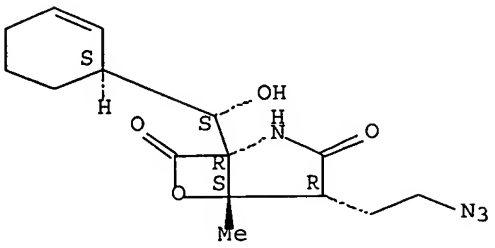
RN 872360-20-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[[(3S)-3-hydroxy-1-cyclohexen-1-yl]carbonyl]-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



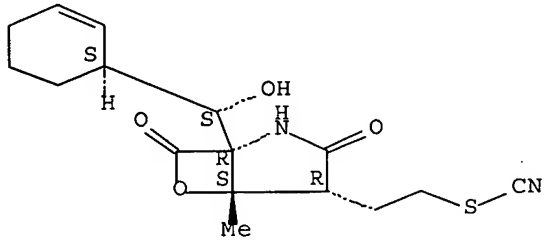
RN 872360-22-0 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-azidoethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



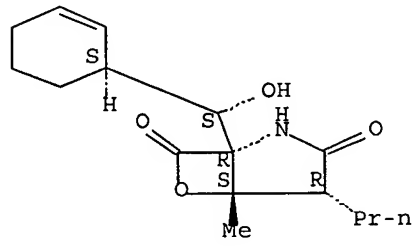
RN 872360-23-1 HCAPLUS
CN Thiocyanic acid, 2-[(1R,4R,5S)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-3,7-dioxo-6-oxa-2-azabicyclo[3.2.0]hept-4-yl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



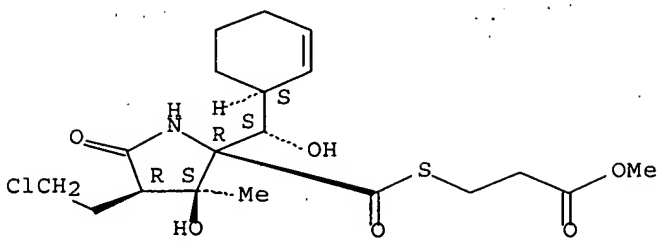
RN 872360-24-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-4-propyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



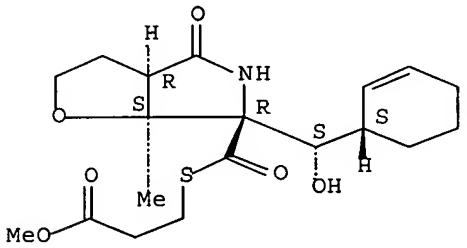
RN 872360-25-3 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



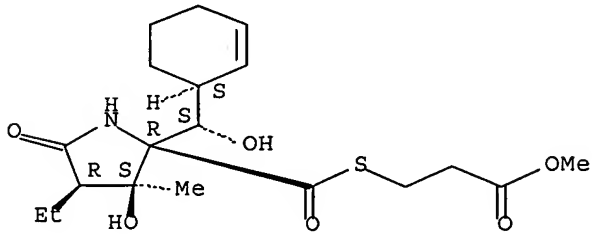
RN 872360-26-4 HCAPLUS
CN Propanoic acid, 3-[[[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrol-6-yl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



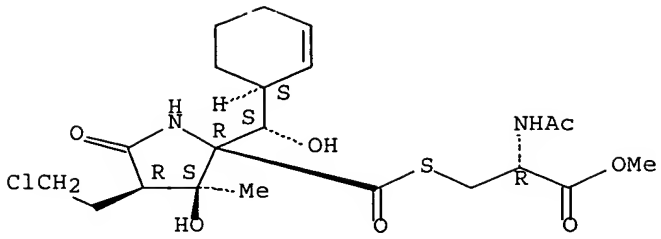
RN 872360-27-5 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 872360-30-0 HCAPLUS
CN L-Cysteine, N-acetyl-S-[(3S,4R)-4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-3-methyl-5-oxo-D-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

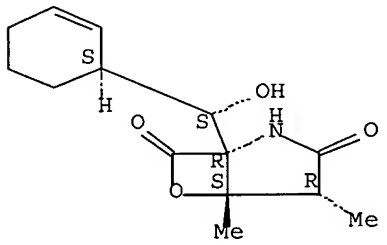
Absolute stereochemistry.



IT **823229-26-1P 872360-12-8P 872360-13-9P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

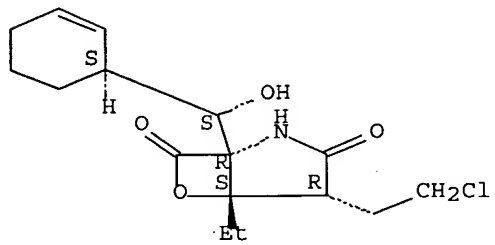
RN 823229-26-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-dimethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 872360-12-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-5-ethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

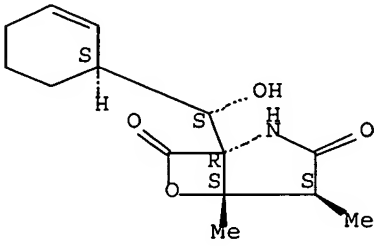
Absolute stereochemistry.



RN 872360-13-9 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-dimethyl-, (1R,4S,5S)- (9CI) (CA INDEX NAME)

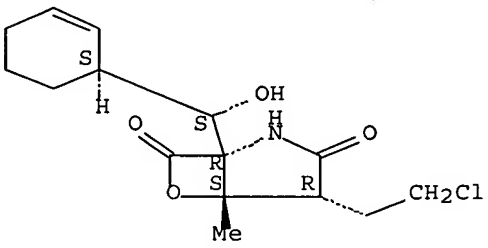
Absolute stereochemistry.



IT **437742-34-2P 863126-95-8P**
RL: **BPN (Biosynthetic preparation)**; RCT (Reactant); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

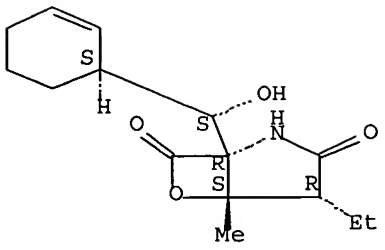
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 863126-95-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

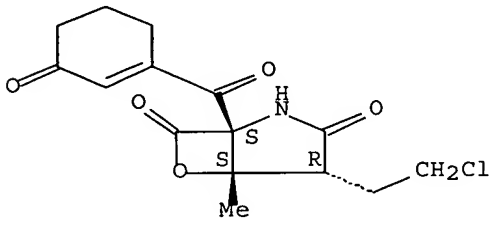


IT **872360-21-9P 872360-29-7P 872360-31-1P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)

RN 872360-21-9 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-5-methyl-1-[(3-oxo-1-cyclohexen-1-yl)carbonyl]-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

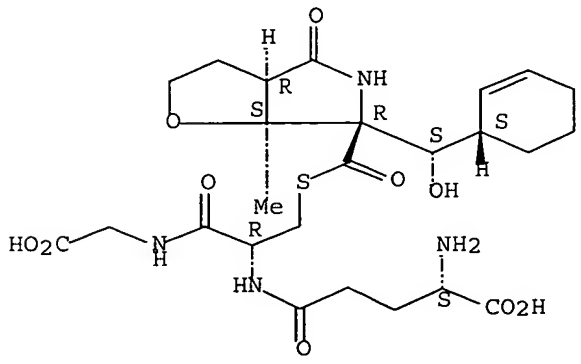
Absolute stereochemistry.



RN 872360-29-7 HCAPLUS

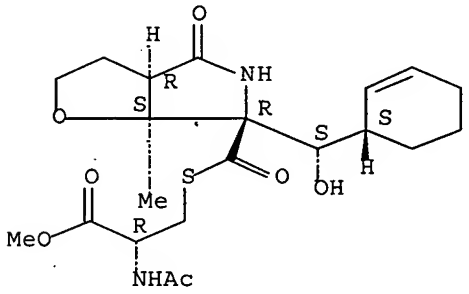
CN Glycine, L-γ-glutamyl-S-[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrole-6-carbonyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



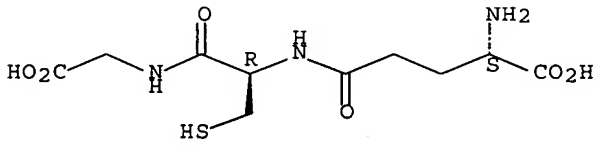
RN 872360-31-1 HCAPLUS
CN L-Cysteine, N-acetyl-S-[[(3aR,6R,6aS)-6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2H-furo[2,3-c]pyrrol-6-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 70-18-8, Glutathione, reactions
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation and MSBAR of oxaazabicycloheptanes obtained via fermentation process
for treatment of cancer, inflammatory conditions, and microbial infections)
RN 70-18-8 HCAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1154365 HCAPLUS Full-text
DOCUMENT NUMBER: 143:422201
TITLE: Preparation of salinosporamide A for use in anticancer pharmaceutical compositions as proteasome inhibitors
INVENTOR(S): Corey, Elias J.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005099687	A2	20051027	WO 2005-US12113	20050411	
WO 2005099687	A3	20051229			

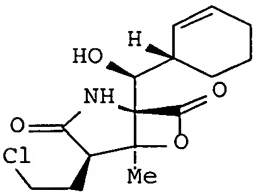
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

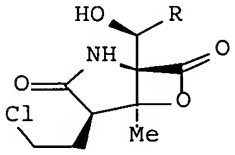
PRIORITY APPLN. INFO.: US 2004-560877P P 20040409

OTHER SOURCE(S): MARPAT 143:422201

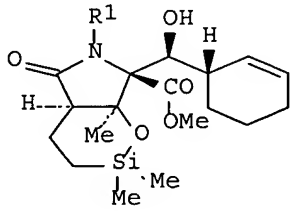
GI



I



II



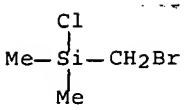
III

AB Salinosporamide A (I) and its analogs, such as II (R = alkyl, alkenyl, etc.), were enantioselectively synthesized starting from N-(4-methoxybenzoyl)-L-threonine Me ester via several novel synthetic intermediates, such as lactam II (R1 = CH2C6H4-4-OMe). The compds. of this invention have been shown to inhibit the proteasome, an intracellular enzyme complex that destroys proteins the cell no longer needs. Without the proteasome, proteins would build up and clog cellular machinery. Fast-growing cancer cells make especially heavy use of the proteasome, so thwarting its action is a compelling drug strategy.

IT **16532-02-8**, (Bromomethyl)chlorodimethylsilane **704910-28-1**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation of salinosporamide A for use in anticancer pharmaceutical compns. as proteasome inhibitors)

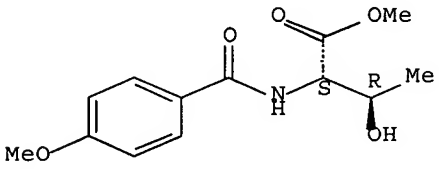
RN 16532-02-8 HCAPLUS

CN Silane, (bromomethyl)chlorodimethyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



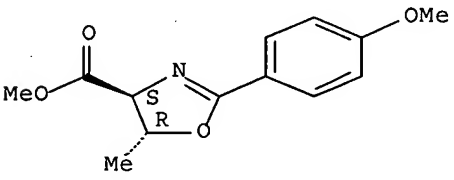
RN 704910-28-1 HCAPLUS
CN L-Threonine, N-(4-methoxybenzoyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



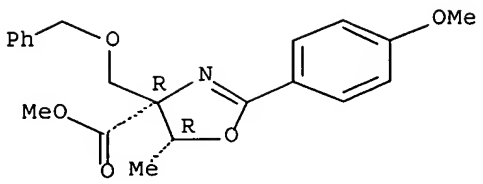
IT **704910-29-2P 704910-30-5P 704910-31-6P**
704910-32-7P 704910-33-8P 704910-34-9P
704910-35-0P 704910-36-1P 704910-37-2P
704910-38-3P 704910-39-4P 704910-41-8P
704910-42-9P 704910-43-0P 704910-44-1P
704910-45-2P 857311-65-0P 857681-75-5P
857681-76-6P 857681-77-7P 857681-80-2P
857681-81-3P 857681-82-4P 857681-83-5P
860453-67-4P 860453-68-5P 860453-69-6P
860453-70-9P 860453-71-0P 860453-72-1P
860453-75-4P 860453-76-5P 860453-77-6P
RL: RCT (Reactant); SPN (Synthetic preparation);
PREP (Preparation); RACT (Reactant or reagent)
(preparation of salinosporamide A for use in anticancer pharmaceutical compns. as proteasome inhibitors)
RN 704910-29-2 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



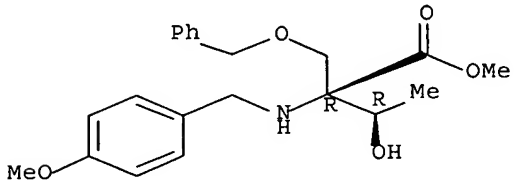
RN 704910-30-5 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-4-[(phenylmethoxy)methyl]-, methyl ester, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



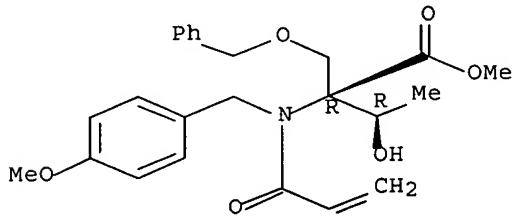
RN 704910-31-6 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



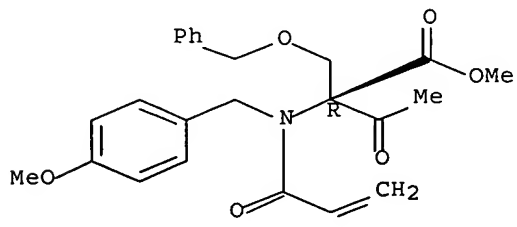
RN 704910-32-7 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



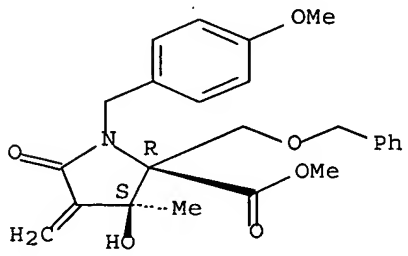
RN 704910-33-8 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



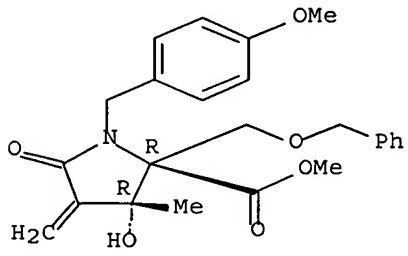
RN 704910-34-9 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



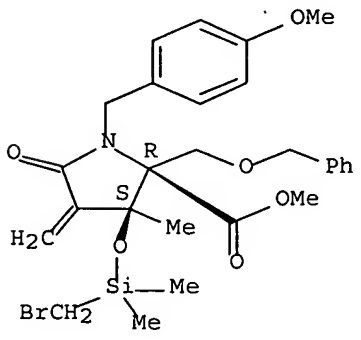
RN 704910-35-0 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



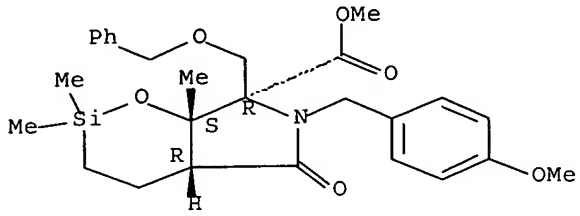
RN 704910-36-1 HCAPLUS
CN D-Proline, 3-[[(bromomethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



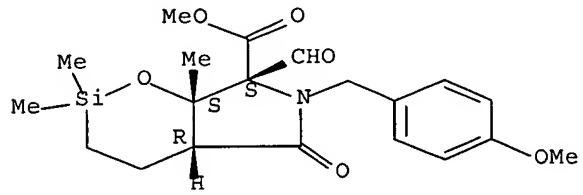
RN 704910-37-2 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-7-[(phenylmethoxy)methyl]-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



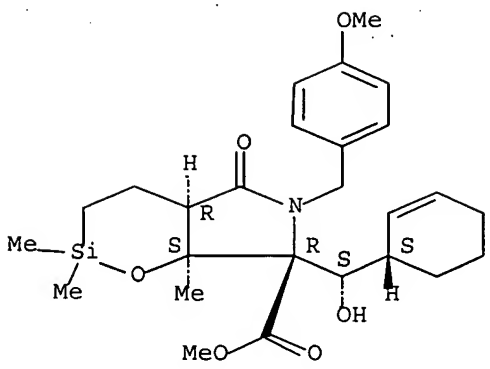
RN 704910-38-3 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-formyloctahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7S,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



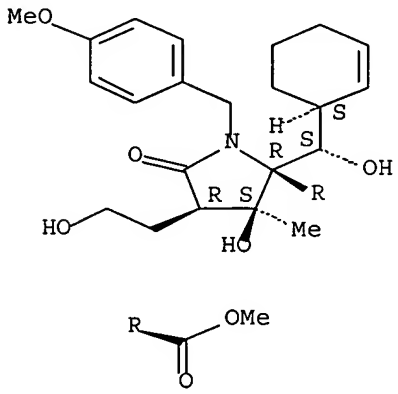
RN 704910-39-4 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



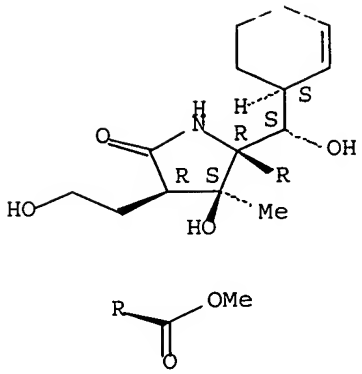
RN 704910-41-8 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



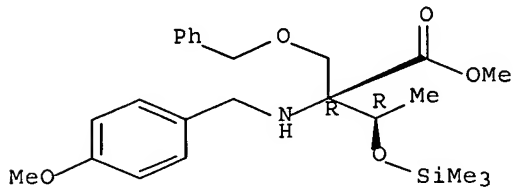
RN 704910-42-9 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



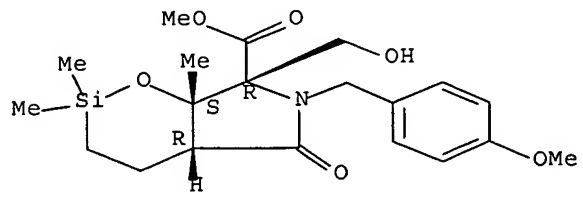
RN 704910-43-0 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-3-[(trimethylsilyl)oxy]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

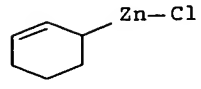


RN 704910-44-1 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-(hydroxymethyl)-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

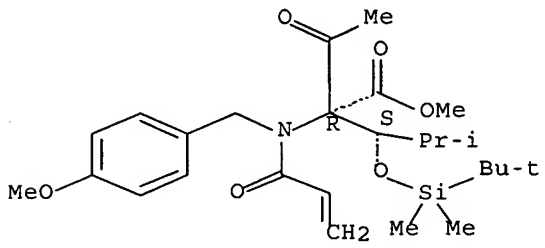


RN 704910-45-2 HCAPLUS
CN Zinc, chloro-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



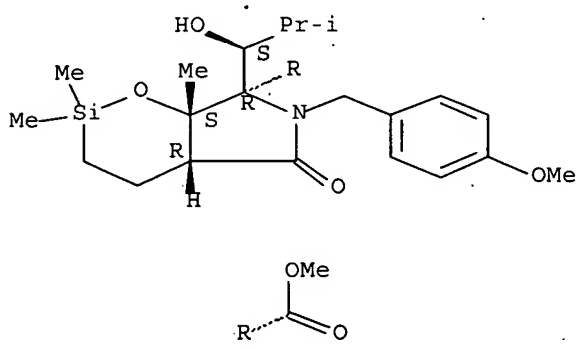
RN 857311-65-0 HCAPLUS
CN L-Leucine, 2-acetyl-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-N-[(4-methoxyphenyl)methyl]-N-(1-oxo-2-propenyl)-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



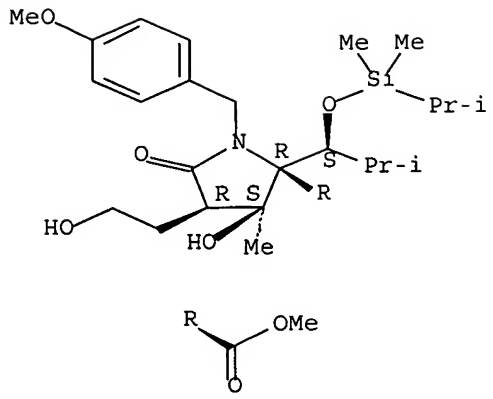
RN 857681-75-5 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-[(1S)-1-hydroxy-2-methylpropyl]-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



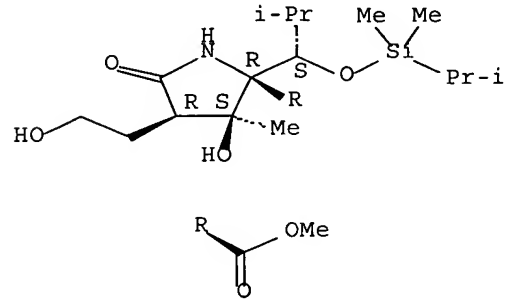
RN 857681-76-6 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[dimethyl(1-methylethyl)silyl]oxy]-2-methylpropyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



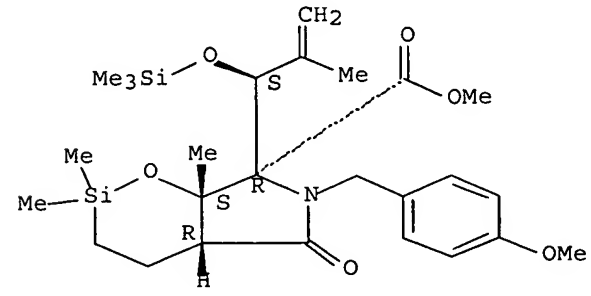
RN 857681-77-7 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[dimethyl(1-methylethyl)silyl]oxy]-2-methylpropyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



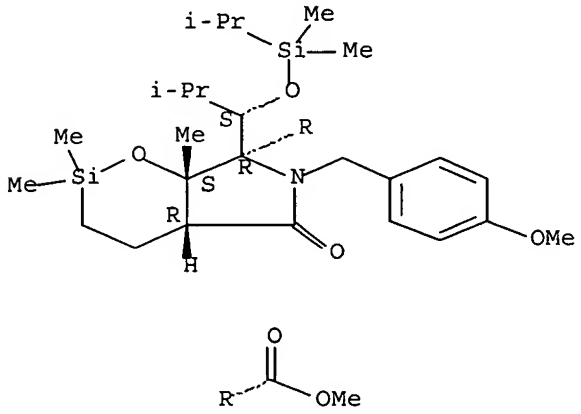
RN 857681-80-2 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-7-[(1S)-2-methyl-1-[(trimethylsilyl)oxy]-2-propenyl]-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



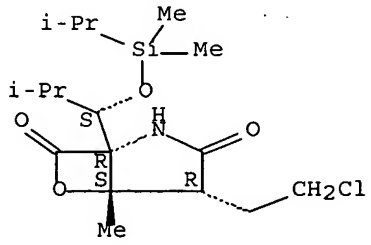
RN 857681-81-3 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(1S)-1-[[dimethyl(1-methylethyl)silyl]oxy]-2-methylpropyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



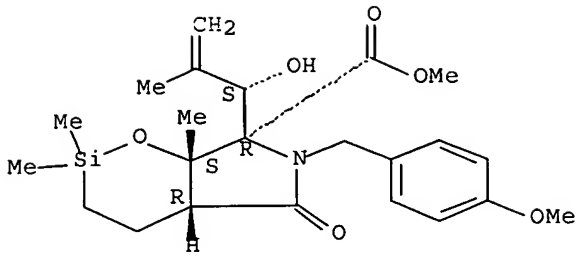
RN 857681-82-4 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(1S)-1-[[dimethyl(1-methylethyl)silyl]oxy]-2-methylpropyl]-5-methyl-, (1R,4R,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



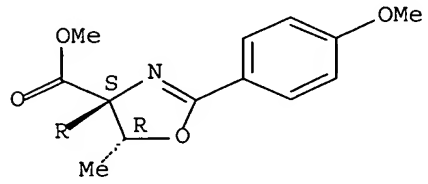
RN 857681-83-5 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-[(1S)-1-hydroxy-2-methyl-2-propenyl]-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

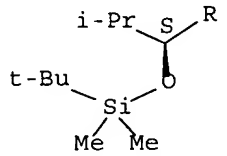
Absolute stereochemistry. Rotation (-).



RN 860453-67-4 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4S,5R)- (9CI) (CA INDEX NAME)

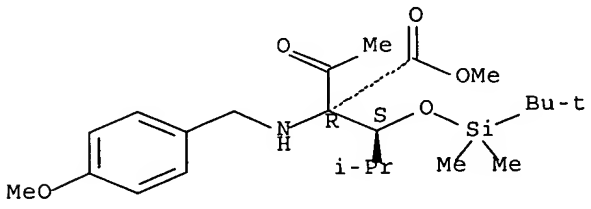
Absolute stereochemistry. Rotation (-).





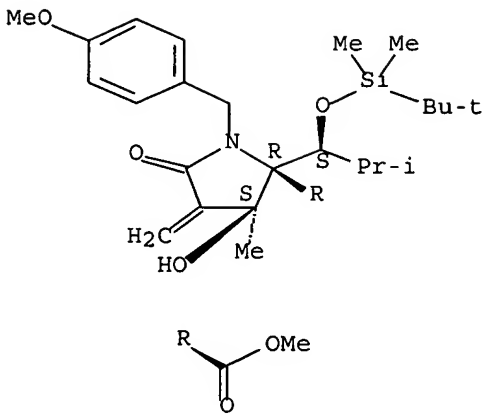
RN 860453-68-5 HCAPLUS
CN L-Leucine, 2-acetyl-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-N-[(4-methoxyphenyl)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



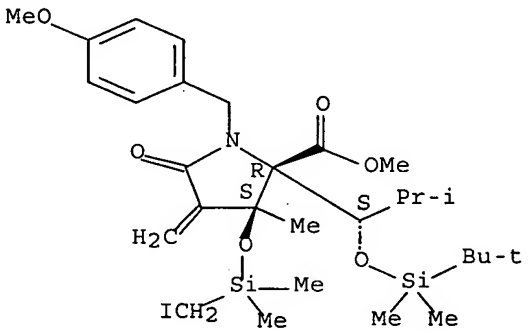
RN 860453-69-6 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



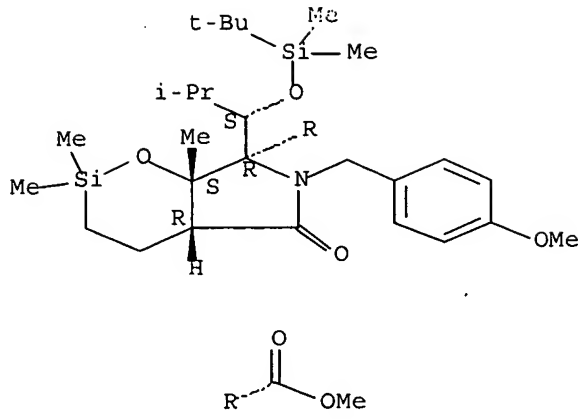
RN 860453-70-9 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-3-[[(iodomethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-, methyl ester, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



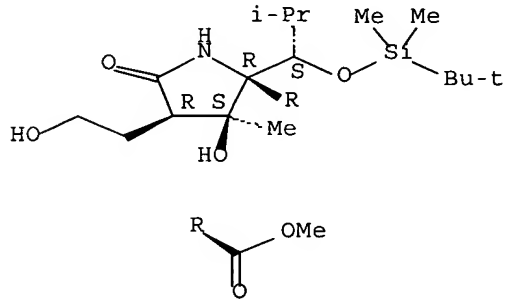
RN 860453-71-0 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



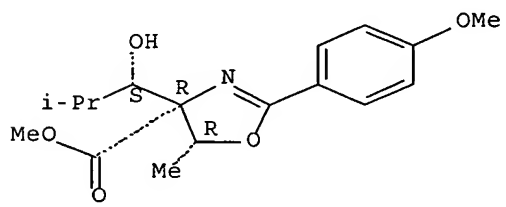
RN 860453-72-1 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 860453-75-4 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-4-[(1S)-1-hydroxy-2-methylpropyl]-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4R,5R)- (9CI) (CA INDEX NAME)

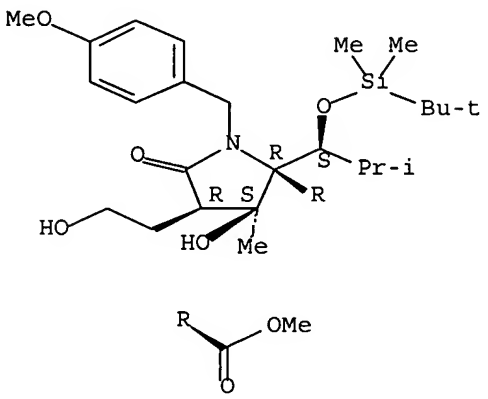
Absolute stereochemistry. Rotation (+).



RN 860453-76-5 HCAPLUS
CN D-Proline, 2-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-

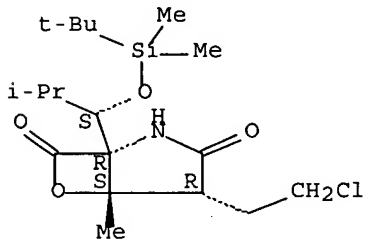
methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



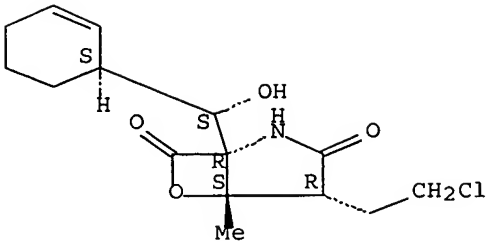
RN 860453-77-6 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(1S)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **437742-34-2P**, (-)-Salinosporamide A
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of salinosporamide A for use in anticancer pharmaceutical compns. as proteasome inhibitors)
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

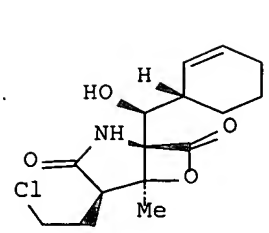


L31 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1106831 HCAPLUS Full-text
DOCUMENT NUMBER: 143:386848
TITLE: Simple stereocontrolled synthesis of salinosporamide A
INVENTOR(S): Corey, Elias J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005228186	A1	20051013	US 2004-821621	20040409
WO 2005113558	A2	20051201	WO 2005-US12218	20050411
WO 2005113558	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-821621 A 20040409
OTHER SOURCE(S): CASREACT 143:386848
GI



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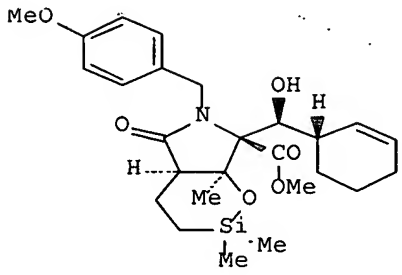


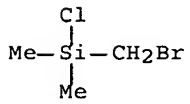
II

AB A simple and effective stereocontrolled synthesis of (-)-salinosporamide A (I) was disclosed. The process, the first total synthesis of salinosporamide A, is capable of providing the compound in substantial quantities for further biol. studies. The disclosed synthetic scheme started from N-(4-methoxybenzoyl)-L-threonine Me ester and included the preparation of several novel synthetic intermediate compds., such as lactam II. Salinosporamide A is a synthetic target of special interest because it has previously shown proteasome inhibiting activity and shown cytotoxic activity in vitro against many tumor cell lines (IC50 values of 10 nM or less).

IT **16532-02-8**, (Bromomethyl)chlorodimethylsilane
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(asym. synthesis of salinosporamide A)

RN 16532-02-8 HCAPLUS

CN Silane, (bromomethyl)chlorodimethyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

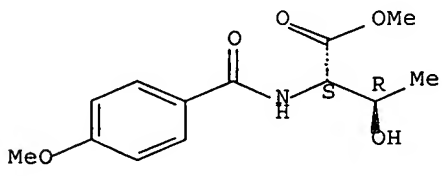


IT **704910-28-1P**, N-(4-Methoxybenzoyl)-L-threonine methyl ester
704910-29-2P 704910-30-5P 704910-31-6P
704910-32-7P 704910-33-8P 704910-34-9P
704910-35-0P 704910-36-1P 704910-37-2P
704910-38-3P 704910-39-4P 704910-41-8P
704910-42-9P 704910-44-1P 704910-45-2P
RL: **RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)**
(asym. synthesis of salinosporamide A)

RN 704910-28-1 HCAPLUS

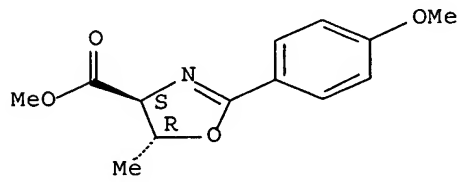
CN L-Threonine, N-(4-methoxybenzoyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



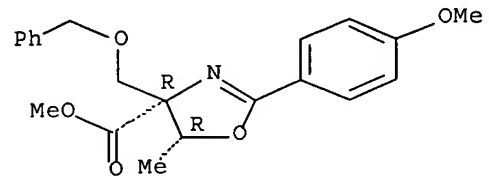
RN 704910-29-2 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



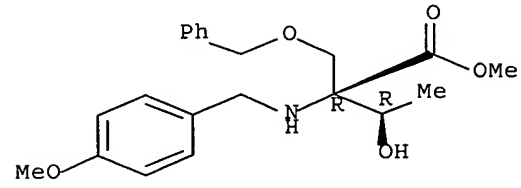
RN 704910-30-5 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-4-[(phenylmethoxy)methyl]-, methyl ester, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



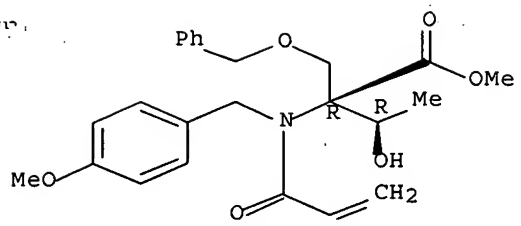
RN 704910-31-6 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



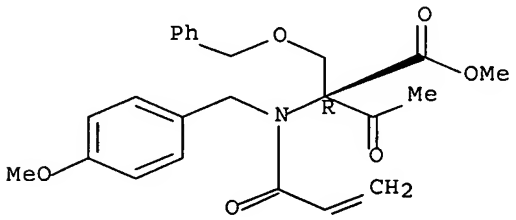
RN 704910-32-7 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



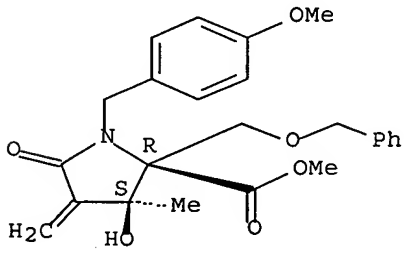
RN 704910-33-8 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



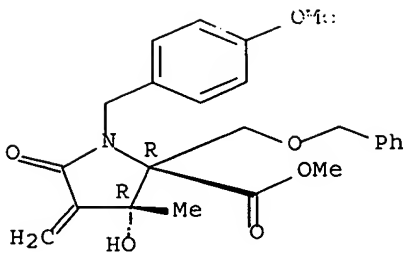
RN 704910-34-9 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



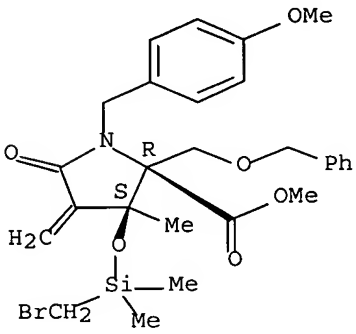
RN 704910-35-0 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



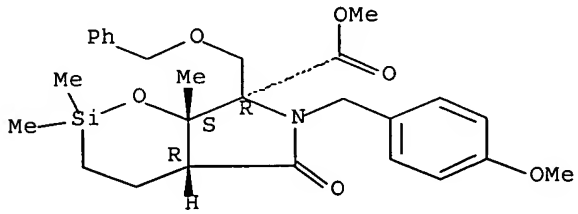
RN 704910-36-1 HCAPLUS
CN D-Proline, 3-[[(bromomethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



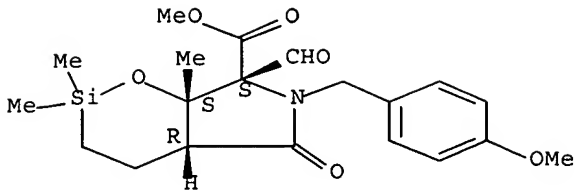
RN 704910-37-2 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-7-[(phenylmethoxy)methyl]-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



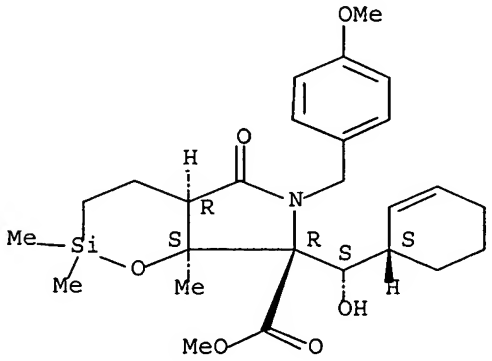
RN 704910-38-3 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-formyloctahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7S,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



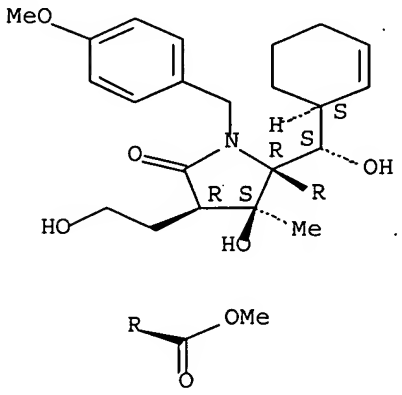
RN 704910-39-4 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



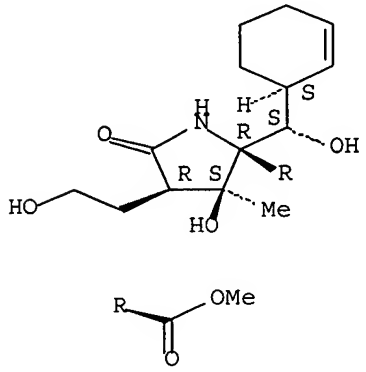
RN 704910-41-8 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



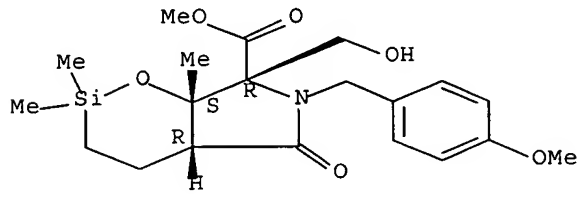
RN 704910-42-9 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

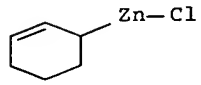


RN 704910-44-1 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-(hydroxymethyl)-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



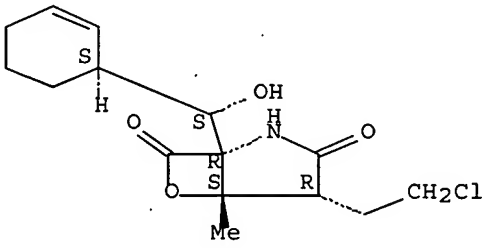
RN 704910-45-2 HCAPLUS
CN Zinc, chloro-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



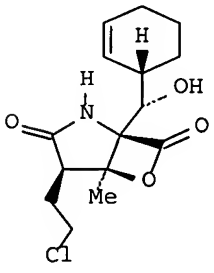
IT **437742-34-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of salinosporamide A)
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-

2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L31 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:421879 HCAPLUS Full-text
DOCUMENT NUMBER: 143:153185
TITLE: Total Synthesis of Salinosporamide A
AUTHOR(S): Endo, Atsushi; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of the American Chemical Society (2005), 127(23), 8298-8299
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:153185
GI

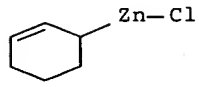


I

AB Total synthesis of potent proteasome inhibitor salinosporamide A (I) has been accomplished, which features strictly substrate-controlled operations starting with the only chiral center of (R)-pyroglutamic acid. The consecutive quaternary carbons within I have been efficiently constructed by manipulation of two intramol. reactions: carbonate-mediated internal acylation of an imidate ester and selenocyclization of aldehyde to exocyclic methylene group.

IT 704910-45-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(total synthesis of salinosporamide A)

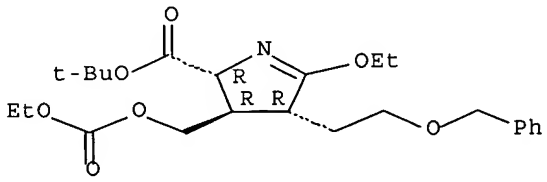
RN 744910-45-2 HCAPLUS
CN Zinc, chloro-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



IT **856681-96-4P 856681-97-5P 856681-98-6P**
856682-02-5P 856682-03-6P 856682-04-7P
856682-05-8P 856682-06-9P 856682-07-0P
856682-08-1P 856682-09-2P 856682-10-5P
856682-11-6P 856682-12-7P 856682-13-8P
856682-14-9P 856682-15-0P 856682-16-1P
856682-20-7P 856682-21-8P 856682-22-9P
856682-23-0P 856682-24-1P 856682-25-2P
856682-26-3P 856682-27-4P
RL: RCT (Reactant); SPN (Synthetic preparation);
PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of salinosporamide A)

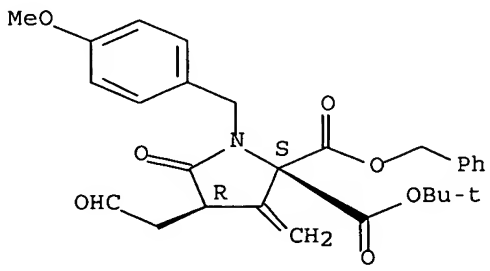
RN 856681-96-4 HCAPLUS
CN 2H-Pyrrole-2-carboxylic acid, 5-ethoxy-3-[[(ethoxycarbonyl)oxy]methyl]-3,4-dihydro-4-[2-(phenylmethoxy)ethyl]-, 1,1-dimethylethyl ester, (2R,3R,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



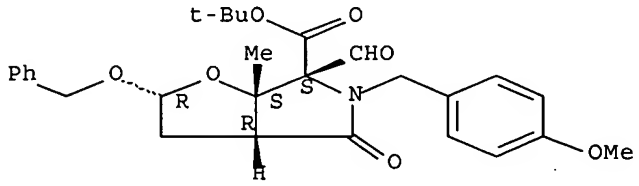
RN 856681-97-5 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 1-[(4-methoxyphenyl)methyl]-3-methylene-5-oxo-4-(2-oxoethyl)-, 1,1-dimethylethyl phenylmethyl ester, (2S,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



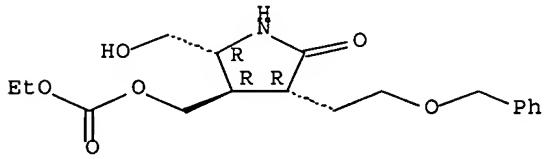
RN 856681-98-6 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-formylhexahydro-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



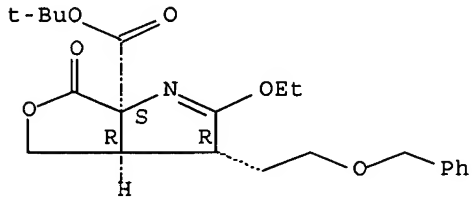
RN 856682-02-5 HCAPLUS
CN Carbonic acid, ethyl [(2R,3R,4R)-2-(hydroxymethyl)-5-oxo-4-[2-(phenylmethoxy)ethyl]-3-pyrrolidinyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



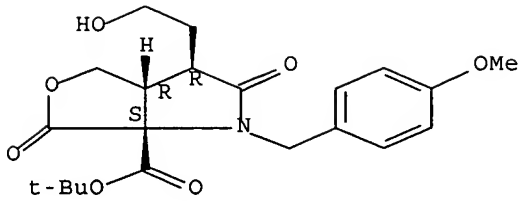
RN 856682-03-6 HCAPLUS
CN 3H-Furo[3,4-b]pyrrole-6a(6H)-carboxylic acid, 2-ethoxy-3a,4-dihydro-6-oxo-3-[2-(phenylmethoxy)ethyl]-, 1,1-dimethylethyl ester, (3R,3aR,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



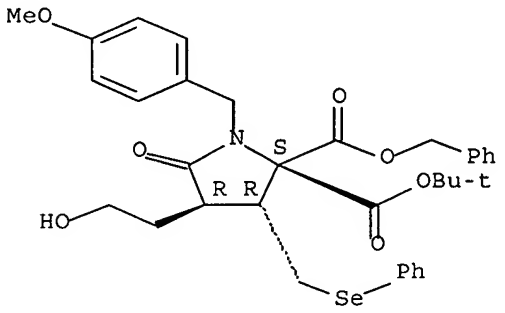
RN 856682-04-7 HCAPLUS
CN 1H-Furo[3,4-b]pyrrole-6a(6H)-carboxylic acid, tetrahydro-3-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-2,6-dioxo-, 1,1-dimethylethyl ester, (3R,3aR,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



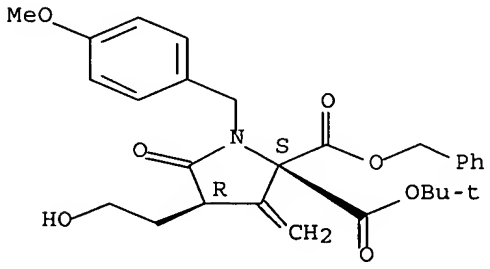
RN 856682-05-8 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-5-oxo-3-[(phenylseleno)methyl]-, 1,1-dimethylethyl phenylmethyl ester, (2S,3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



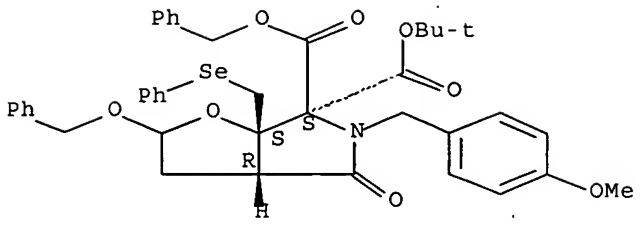
RN 856682-06-9 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methylene-5-oxo-, 1,1-dimethylethyl phenylmethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



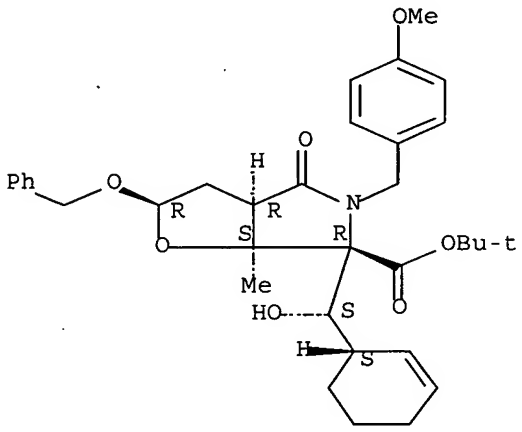
RN 856682-07-0 HCAPLUS
CN 6H-Furo[2,3-c]pyrrole-6,6-dicarboxylic acid, hexahydro-5-[(4-methoxyphenyl)methyl]-4-oxo-2-(phenylmethoxy)-6a-[(phenylseleno)methyl]-, 1,1-dimethylethyl phenylmethyl ester, (3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



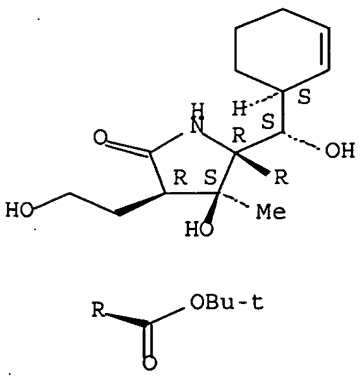
RN 856682-08-1 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



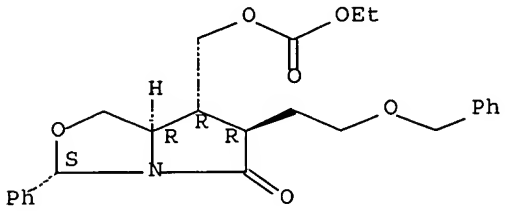
RN 856682-09-2 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, 1,1-dimethylethyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



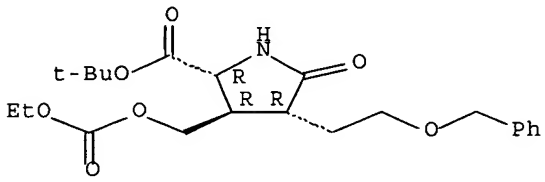
RN 856682-10-5 HCAPLUS
CN Carbonic acid, ethyl [(3S,6R,7R,7aR)-tetrahydro-5-oxo-3-phenyl-6-[2-(phenylmethoxy)ethyl]-1H,3H-pyrrolo[1,2-c]oxazol-7-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



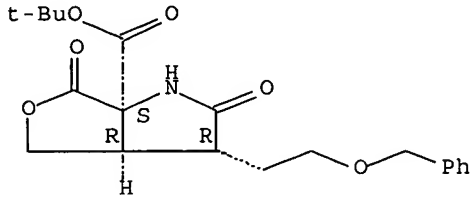
RN 856682-11-6 HCAPLUS
CN D-Proline, 3-[[(ethoxycarbonyl)oxy]methyl]-5-oxo-4-[2-(phenylmethoxy)ethyl]-, 1,1-dimethylethyl ester, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 856682-12-7 HCAPLUS
CN 1H-Furo[3,4-b]pyrrole-6a(6H)-carboxylic acid, tetrahydro-2,6-dioxo-3-[2-(phenylmethoxy)ethyl]-, 1,1-dimethylethyl ester, (3R,3aR,6aS)- (9CI) (CA INDEX NAME)

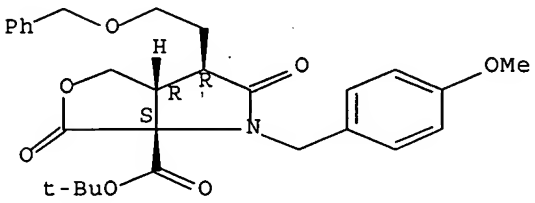
Absolute stereochemistry. Rotation (+).



RN 856682-13-8 HCAPLUS
CN 1H-Furo[3,4-b]pyrrole-6a(6H)-carboxylic acid, tetrahydro-1-[(4-methoxyphenyl)methyl]-2,6-dioxo-3-[2-(phenylmethoxy)ethyl]-,

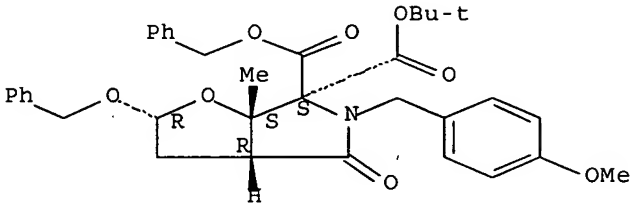
1,1-dimethylethyl ester, (3R,3aR,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



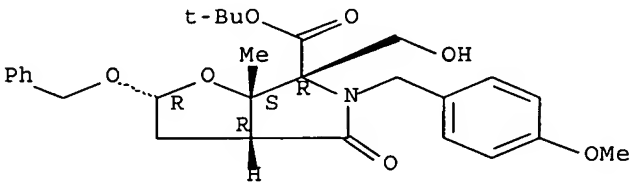
RN 856682-14-9 HCAPLUS
CN 6H-Furo[2,3-c]pyrrole-6,6-dicarboxylic acid, hexahydro-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl phenylmethyl ester, (2R,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



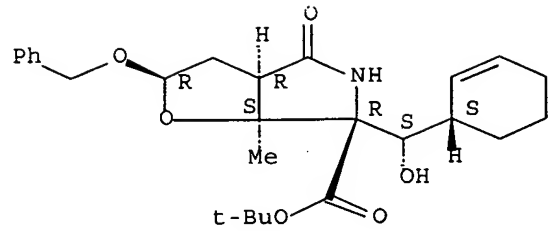
RN 856682-15-0 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, hexahydro-6-(hydroxymethyl)-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



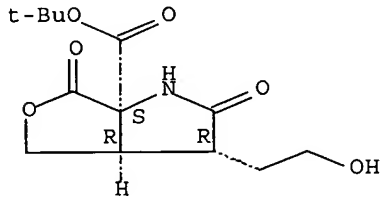
RN 856682-16-1 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



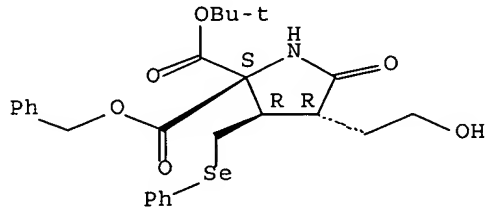
RN 856682-20-7 HCAPLUS
CN 1H-Furo[3,4-b]pyrrole-6a(6H)-carboxylic acid, tetrahydro-3-(2-hydroxyethyl)-2,6-dioxo-, 1,1-dimethylethyl ester, (3R,3aR,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



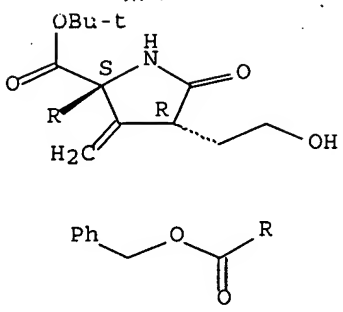
RN 856682-21-8 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 4-(2-hydroxyethyl)-5-oxo-3-[(phenylseleno)methyl]-, 1,1-dimethylethyl phenylmethyl ester, (2S,3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



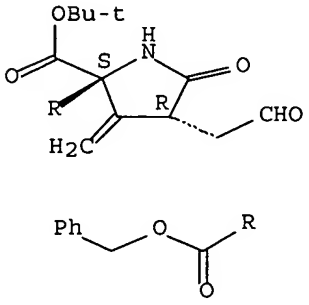
RN 856682-22-9 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 4-(2-hydroxyethyl)-3-methylene-5-oxo-, 1,1-dimethylethyl phenylmethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



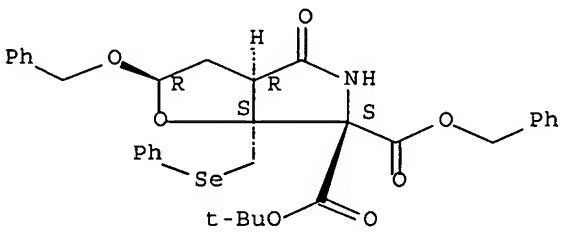
RN 856682-23-0 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 3-methylene-5-oxo-4-(2-oxoethyl)-, 1,1-dimethylethyl phenylmethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



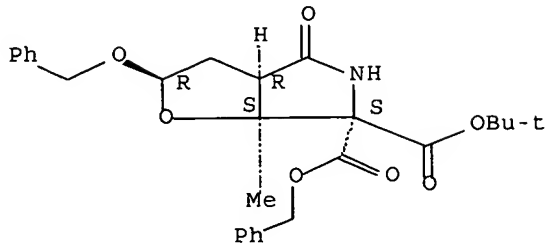
RN 856682-24-1 HCAPLUS
CN 6H-Furo[2,3-c]pyrrole-6,6-dicarboxylic acid, hexahydro-4-oxo-2-(phenylmethoxy)-6a-[(phenylseleno)methyl]-, 1,1-dimethylethyl phenylmethyl ester, (2R,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



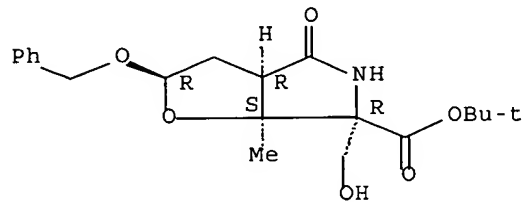
RN 856682-25-2 HCAPLUS
CN 6H-Furo[2,3-c]pyrrole-6,6-dicarboxylic acid, hexahydro-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl phenylmethyl ester, (2R,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



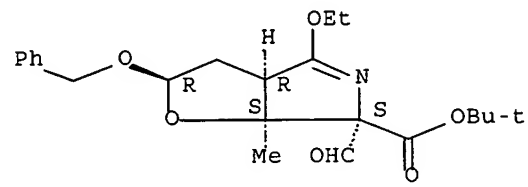
RN 856682-26-3 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, hexahydro-6-(hydroxymethyl)-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



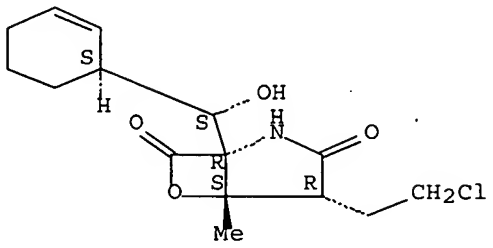
RN 856682-27-4 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 4-ethoxy-6-formyl-3,3a,6,6a-tetrahydro-6a-methyl-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



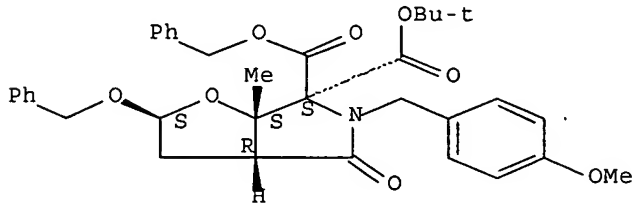
IT **437742-34-2P 856682-18-3P 856682-19-4P 856682-28-5P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(total synthesis of salinosporamide A)
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



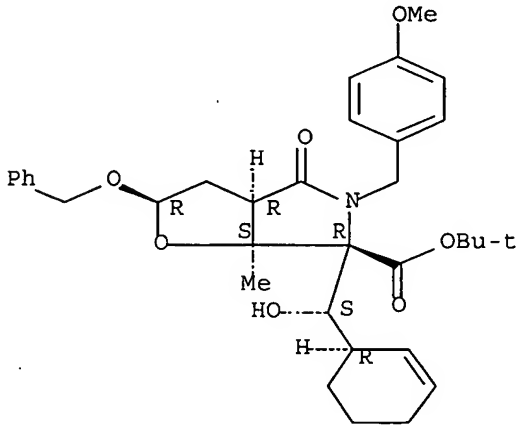
RN 856682-18-3 HCAPLUS
CN 6H-Furo[2,3-c]pyrrole-6,6-dicarboxylic acid, hexahydro-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl phenylmethyl ester, (2S,3aR,6S,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



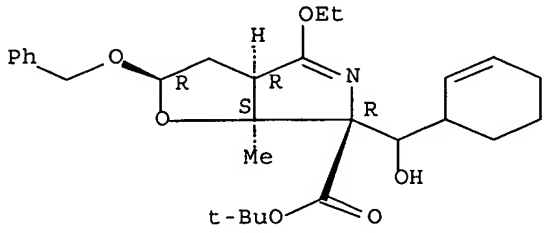
RN 856682-19-4 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-[(S)-(1R)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-5-[(4-methoxyphenyl)methyl]-6a-methyl-4-oxo-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 856682-28-5 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-(2-cyclohexen-1-ylhydroxymethyl)-4-ethoxy-3,3a,6,6a-tetrahydro-6a-methyl-2-(phenylmethoxy)-, 1,1-dimethylethyl ester, (2R,3aR,6R,6aS)- (9CI) (CA INDEX NAME)

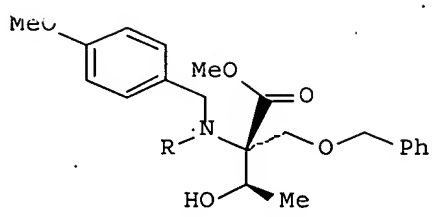
Absolute stereochemistry.



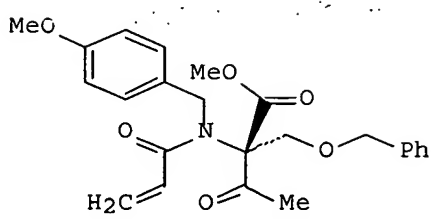
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:340603 HCAPLUS Full-text
DOCUMENT NUMBER: 141:54117
TITLE: A Simple Stereocontrolled Synthesis of Salinosporamide A
AUTHOR(S): Reddy, Leleti Rajender; Saravanan, P.; Corey, E. J.
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (2004), 126(20), 6230-6231
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:54117
GI

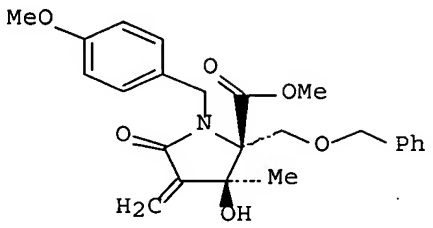
4/9/54



I



II



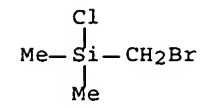
III

AB A simple and effective stereocontrolled synthesis of salinosporamide A has been developed. Of special note is the direct conversion of amino(benzyloxymethyl)hydroxybutanoate I (R = H) to acryloyl derivative I (R = COCH:CH2). Also, quinuclidine proved to be superior to other bases in the cyclization of oxybutanoate II to oxopyrrolidinecarboxylate III. This process, the first synthesis of salinosporamide A, is capable of providing the compound in substantial quantities for further biol. studies. Salinosporamide A was of special interest as a synthetic target because of its potent in vitro cytotoxic activity against many tumor cell lines (IC50 values of 10 nM or less).

IT 16532-02-8, Bromomethyldimethylchlorosilane
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(asym. synthesis of salinosporamide A)

RN 16532-02-8 HCAPLUS

CN Silane, (bromomethyl)chlorodimethyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

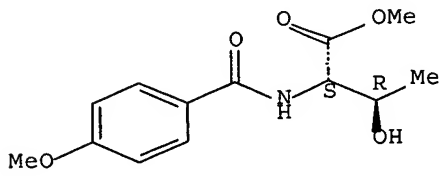


IT **704910-28-1P 704910-29-2P 704910-30-5P**
704910-31-6P 704910-32-7P 704910-33-8P
704910-34-9P 704910-36-1P 704910-37-2P
704910-38-3P 704910-39-4P 704910-41-8P
704910-42-9P 704910-43-0P 704910-44-1P
704910-45-2P
RL: **RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)**
(asym. synthesis of salinosporamide A)

RN 704910-28-1 HCAPLUS

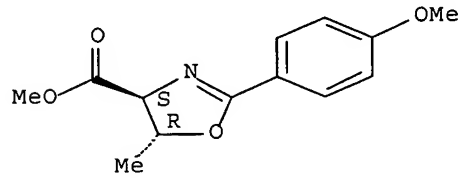
CN L-Threonine, N-(4-methoxybenzoyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



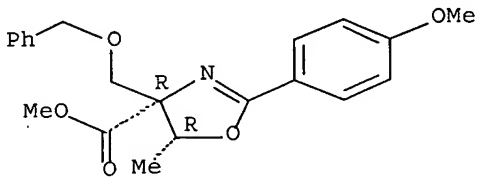
RN 704910-29-2 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-, methyl ester, (4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



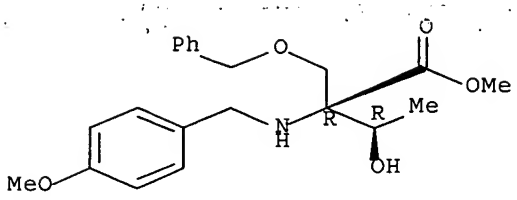
RN 704910-30-5 HCAPLUS
CN 4-Oxazolecarboxylic acid, 4,5-dihydro-2-(4-methoxyphenyl)-5-methyl-4-[(phenylmethoxy)methyl]-, methyl ester, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



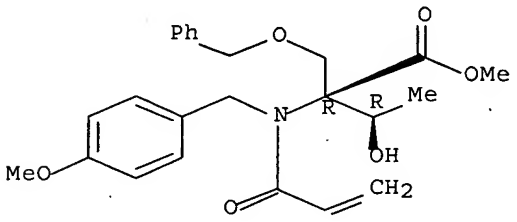
RN 704910-31-6 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



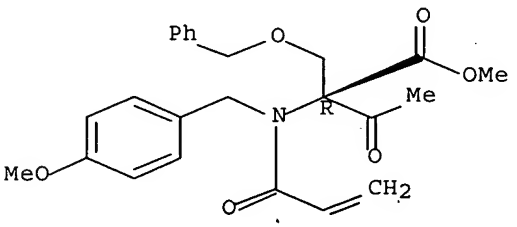
RN 704910-32-7 HCAPLUS
CN D-Isovaline, 3-hydroxy-N-[(4-methoxyphenyl)methyl]-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



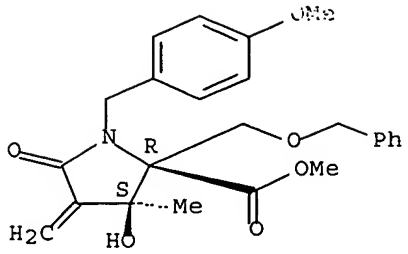
RN 704910-33-8 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-3-oxo-N-(1-oxo-2-propenyl)-2'-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



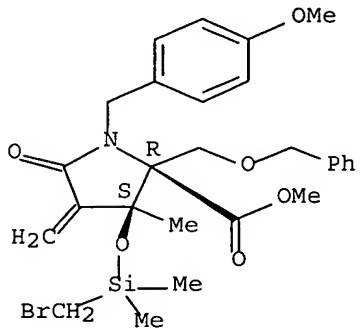
RN 704910-34-9 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



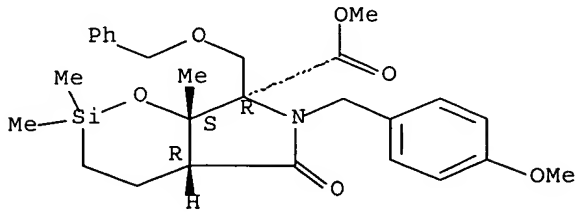
RN 704910-36-1 HCAPLUS
CN D-Proline, 3-[[(bromomethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



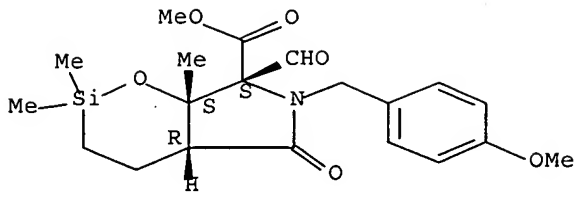
RN 704910-37-2 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-7-[(phenylmethoxy)methyl]-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



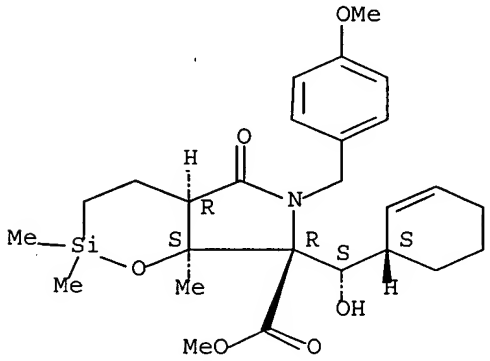
RN 704910-38-3 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-formyloctahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7S,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



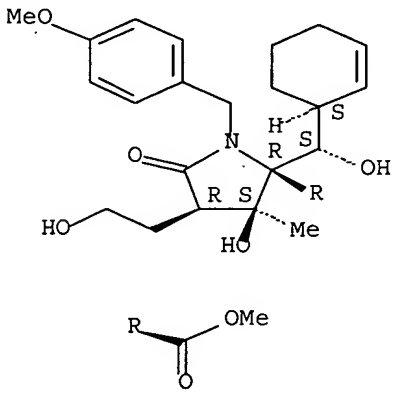
RN 704910-39-4 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, 7-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]octahydro-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



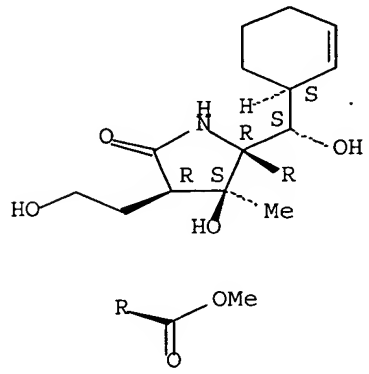
RN 704910-41-8 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-1-[(4-methoxyphenyl)methyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



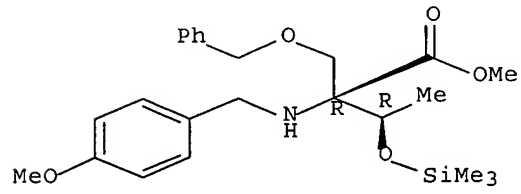
RN 704910-42-9 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(2-hydroxyethyl)-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



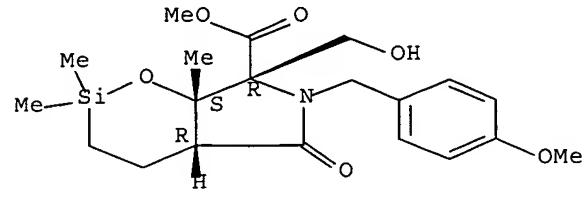
RN 704910-43-0 HCAPLUS
CN D-Isovaline, N-[(4-methoxyphenyl)methyl]-2'-(phenylmethoxy)-3-[(trimethylsilyl)oxy]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

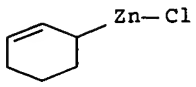


RN 704910-44-1 HCAPLUS
CN 1,2-Oxasilino[5,6-c]pyrrole-7-carboxylic acid, octahydro-7-(hydroxymethyl)-6-[(4-methoxyphenyl)methyl]-2,2,7a-trimethyl-5-oxo-, methyl ester, (4aR,7R,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

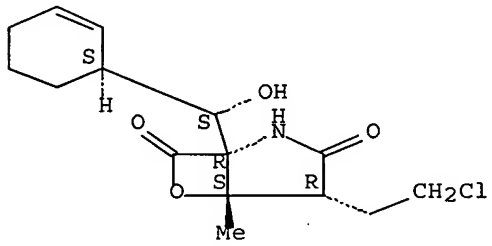


RN 704910-45-2 HCAPLUS
CN Zinc, chloro-2-cyclohexen-1-yl- (9CI) (CA INDEX NAME)



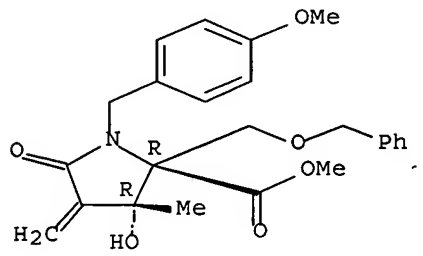
IT **437742-34-2P**, Salinosporamide A **704910-35-0P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(asym. synthesis of salinosporamide A)
RN 437742-34-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 704910-35-0 HCAPLUS
CN D-Proline, 3-hydroxy-1-[(4-methoxyphenyl)methyl]-3-methyl-4-methylene-5-oxo-2-[(phenylmethoxy)methyl]-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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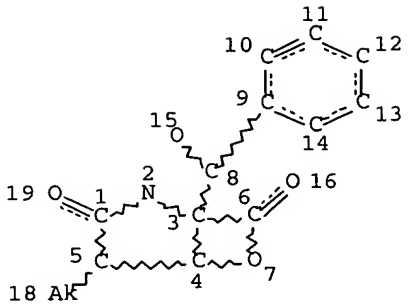

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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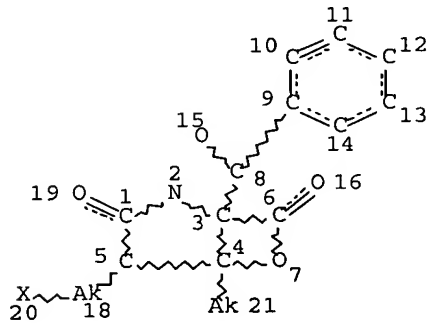
L7 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)PREP+NT/RL
L8 STR



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=> d l32 ibib abs hitstr 1-4

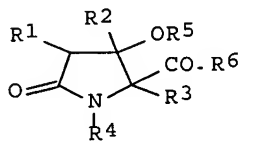
L32 ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:54100  HCAPLUS  Full-text
DOCUMENT NUMBER:          144:128796
TITLE:                    Preparation of substituted 2-pyrrolidone derivatives
                          for use as agrochemical fungicides and insecticides
```

INVENTOR(S): Hillebrand, Stefan; Gueth, Oliver; Wiese, Welf-Burkhard; Kunz, Klaus; Ullmann, Astrid; Mattes, Amos; Schreier, Peter; Wachendorff-Neumann, Ulrike; Kuck, Karl-Heinz; Loesel, Peter; Malsam, Olga; Reinemer, Peter; Stadler, Marc; Seip, Stephan; Mayer-Bartschmid, Anke; Mueller, Hartwig; Bacon, Kevin
PATENT ASSIGNEE(S): Bayer Cropscience A.-G., Germany
SOURCE: PCT Int. Appl., 303 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006005551	A1	20060119	WO 2005-EP7442	20050709

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2004-16320 A 20040712
OTHER SOURCE(S): MARPAT 144:128796
GI



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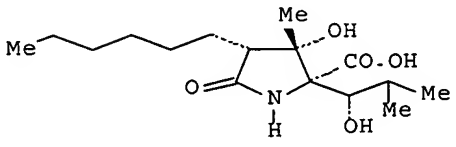


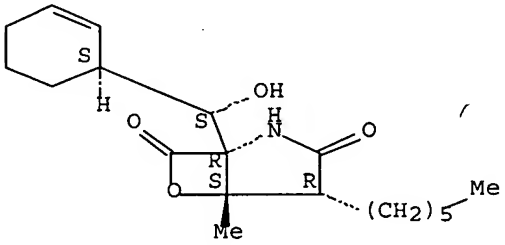
II

AB 2-Pyrrolidone derivs., such as I [R1 = H, halogen, alkyl, alkenyl, alkynyl aryl, heterocyclyl, cycloalkyl, etc.; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl; R3 = H, alkyl, alkenyl, alkynyl, etc.; R4 = H, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, etc.; R5 = H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl; R6 = OR, SR, NRR'; R, R' = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl; R5R6 = bond], were prepared for use as argochems. for the control of insects and phytopathogenic plant fungi. Thus, 4R-hexyl-3S-hydroxy-2R-(1S-hydroxy- 2-methylpropyl)-3-methyl-5-oxopyrrolidine-2-carboxylic acid (II) via a multistep synthesis starting from Me 5S-isopropyl-2-phenyl-4,5-dihydro-1,3- oxazole-4R-carboxylate and Me 2-acetyloctanoate. The prepared pyrrolidones were tested for activity against Podosphaera leucotricha, Venturia inaequalis, Botrytis cinerea, Phytophthora infestans, and Spodoptera frugiperda.
IT **744200-66-6P 744200-67-7P 744200-69-9P 744200-72-4P 744215-21-2P 744215-22-3P**
RL: AGR (Agricultural use); **BPN (Biosynthetic preparation)**; BIOL

(Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 2-pyrrolidone derivs. as agrochem. fungicides and insecticides)

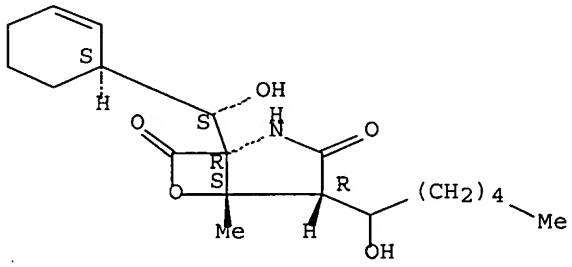
RN 744200-66-6 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



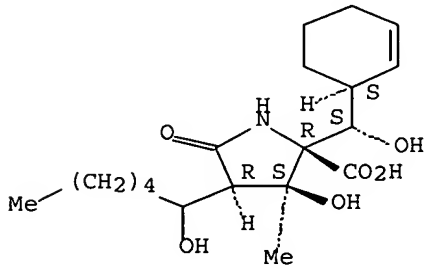
RN 744200-67-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(1-hydroxyhexyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



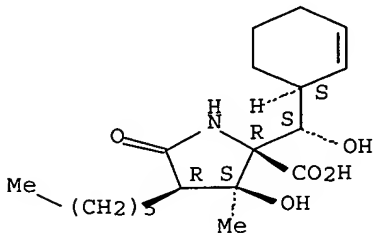
RN 744200-69-9 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(1-hydroxyhexyl)-3-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



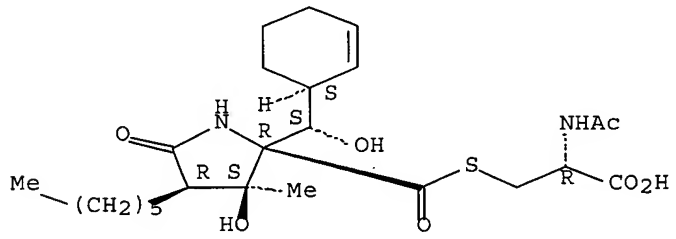
RN 744200-72-4 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



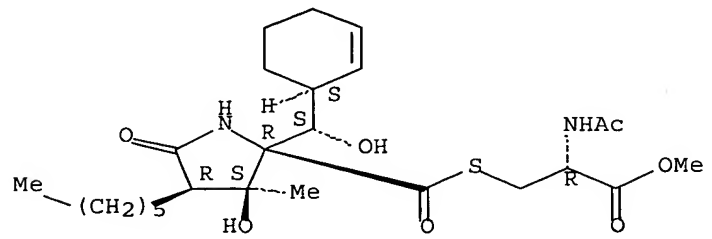
RN 744215-21-2 HCAPLUS
CN L-Cysteine, N-acetyl-, (2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 744215-22-3 HCAPLUS
CN L-Cysteine, N-acetyl-, methyl ester, (2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

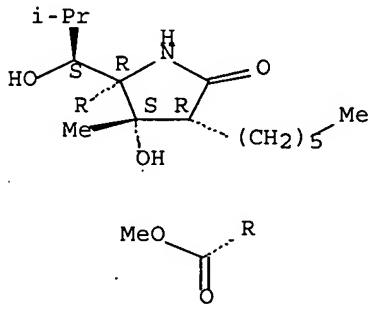
Absolute stereochemistry.



IT **873566-89-3P 873566-91-7P 873566-94-0P,**
4R-Hexyl-3S-hydroxy-2R-(1S-hydroxy-2-methylpropyl)-3-methyl-5-oxopyrrolidine-2-carboxylic acid 873566-95-1P
873566-99-5P 873567-00-1P
RL: AGR (Agricultural use); **RCT (Reactant)**; **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**; **RACT (Reactant or reagent)**; USES (Uses)
(preparation of substituted 2-pyrrolidone derivs. for use as agrochem. fungicides and insecticides)

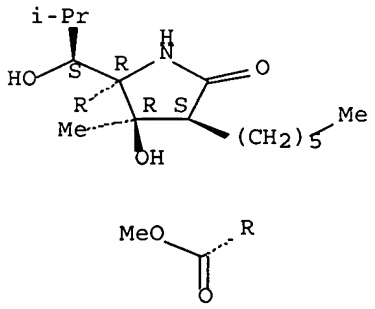
RN 873566-89-3 HCAPLUS
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



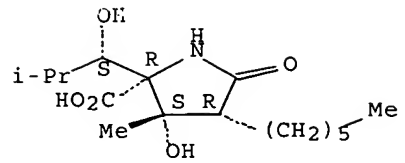
RN 873566-91-7 HCAPLUS
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, methyl ester, (3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



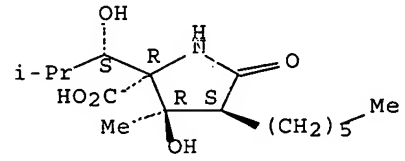
RN 873566-94-0 HCAPLUS
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

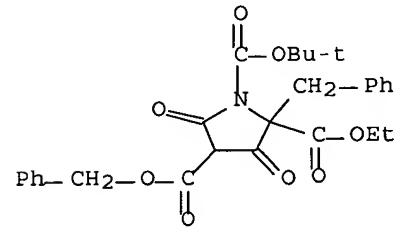


RN 873566-95-1 HCAPLUS
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, (3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

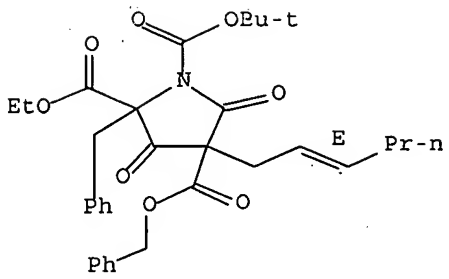


RN 873566-99-5 HCAPLUS
CN 1,2,4-Pyrrolidinetricarboxylic acid, 3,5-dioxo-2-(phenylmethyl)-, 1-(1,1-dimethylethyl) 2-ethyl 4-(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 873567-00-1 HCAPLUS
CN 1,2,4-Pyrrolidinetricarboxylic acid, 4-(2E)-2-hexenyl-3,5-dioxo-2-(phenylmethyl)-, 1-(1,1-dimethylethyl) 2-ethyl 4-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

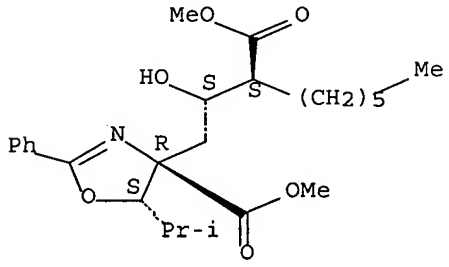


IT 873566-85-9P 873567-01-2P 873567-02-3P
873690-57-4P
RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 2-pyrrolidone derivs. for use as agrochem. fungicides and insecticides)

RN 873566-85-9 HCAPLUS

CN 4-Oxazolebutanoic acid, α-hexyl-4,5-dihydro-β-hydroxy-4-(methoxycarbonyl)-5-(1-methylethyl)-2-phenyl-, methyl ester, (αS,βS,4R,5S)- (9CI) (CA INDEX NAME)

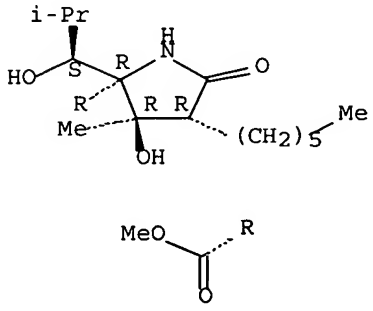
Absolute stereochemistry.



RN 873567-01-2 HCAPLUS

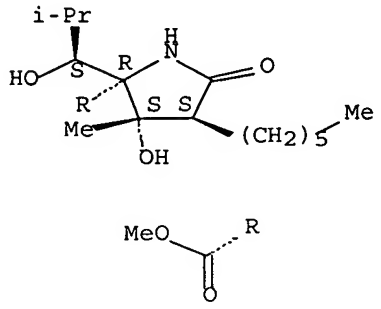
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, methyl ester, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



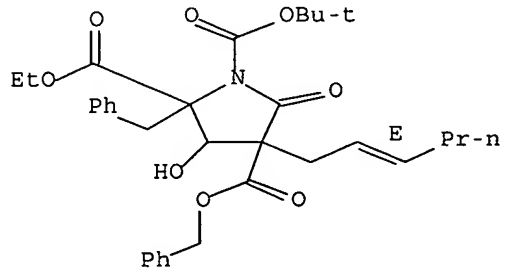
RN 873567-02-3 HCAPLUS
CN D-Proline, 4-hexyl-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-3-methyl-5-oxo-, methyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

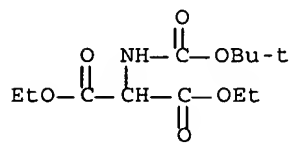


RN 873690-57-4 HCAPLUS
CN 1,2,4-Pyrrolidinetricarboxylic acid, 4-(2E)-2-hexenyl-3-hydroxy-5-oxo-2-(phenylmethyl)-, 1-(1,1-dimethylethyl) 2-ethyl 4-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

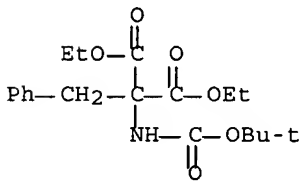


IT 102831-44-7, Diethyl 2-(tert-butoxycarbonylamino)malonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 2-pyrrolidone derivs. for use as agrochem. fungicides and insecticides)
RN 102831-44-7 HCAPLUS
CN Propanedioic acid, [[(1,1-dimethylethoxy)carbonyl]amino]-, diethyl ester (9CI) (CA INDEX NAME)



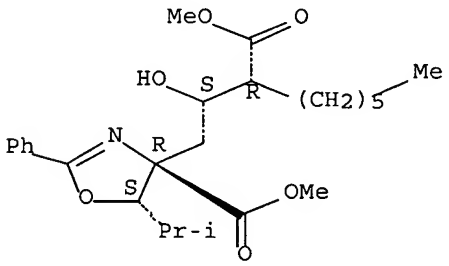
IT 518314-53-9P 873566-86-0P 873566-87-1P
873566-88-2P 873566-98-4P
RL: RCT (Reactant); SPN (Synthetic preparation);
PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted 2-pyrrolidone derivs. for use as agrochem. fungicides and insecticides)

RN 518314-53-9 HCAPLUS
CN Propanedioic acid, [[(1,1-dimethylethoxy)carbonyl]amino](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



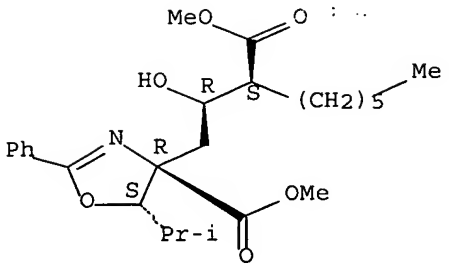
RN 873566-86-0 HCAPLUS
CN 4-Oxazolebutanoic acid, α-hexyl-4,5-dihydro-β-hydroxy-4-(methoxycarbonyl)-5-(1-methylethyl)-2-phenyl-, methyl ester, (αR,βS,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



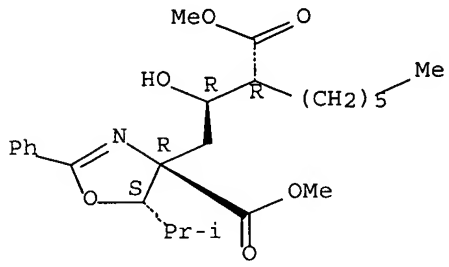
RN 873566-87-1 HCAPLUS
CN 4-Oxazolebutanoic acid, α-hexyl-4,5-dihydro-β-hydroxy-4-(methoxycarbonyl)-5-(1-methylethyl)-2-phenyl-, methyl ester, (αS,βR,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

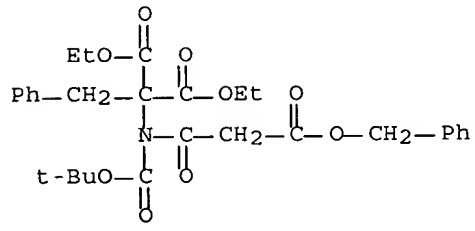


RN 873566-88-2 HCAPLUS
CN 4-Oxazolebutanoic acid, α-hexyl-4,5-dihydro-β-hydroxy-4-(methoxycarbonyl)-5-(1-methylethyl)-2-phenyl-, methyl ester, (αR,βR,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 873566-98-4 HCAPLUS
CN Propanedioic acid, [[(1,1-dimethylethoxy)carbonyl][1,3-dioxo-3-(phenylmethoxy)propyl]amino](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:383219 HCAPLUS Full-text
DOCUMENT NUMBER: 143:70990
TITLE: Structure-Activity Relationship Studies of

Salinosporamide A (NPI-0052), a Novel Marine Derived Proteasome Inhibitor

AUTHOR(S): Macherla, Venkat R.; Mitchell, Scott S.; Manam, Rama Rao; Reed, Katherine A.; Chao, Ta-Hsiang; Nicholson, Benjamin; Deyanat-Yazdi, Gordafaried; Mai, Bao; Jensen, Paul R.; Fenical, William F.; Neuteboom, Saskia T. C.; Lam, Kin S.; Palladino, Michael A.; Potts, Barbara C. M.

CORPORATE SOURCE: Nereus Pharmaceuticals, Inc., San Diego, CA, 92121, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(11), 3684-3687
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:70990

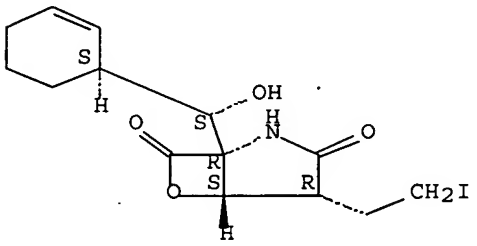
AB Salinosporamide A (1, NPI-0052) is a potent proteasome inhibitor in development for treating cancer. In this study, a series of analogs was assayed for cytotoxicity, proteasome inhibition, and inhibition of NF-κB activation. Marked redns. in potency in cell-based assays accompanied replacement of the chloroethyl group with unhalogenated substituents. Halogen exchange and cyclohexene ring epoxidn. were well tolerated, while some stereochem. modifications significantly attenuated activity. These findings provide insights into structure-activity relationships within this novel series.

IT **855517-18-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(structure-activity relationship studies of salinosporamide A (NPI-0052), a novel marine derived proteasome inhibitor)

RN 855517-18-9 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-iodoethyl)-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

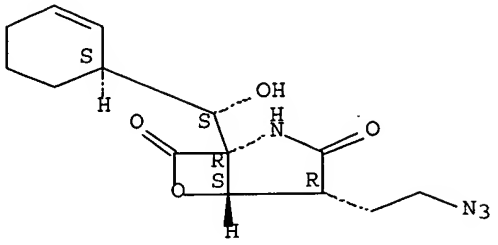


IT **855517-19-0P 855517-20-3P 855517-21-4P**
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(structure-activity relationship studies of salinosporamide A (NPI-0052), a novel marine derived proteasome inhibitor)

RN 855517-19-0 HCAPLUS

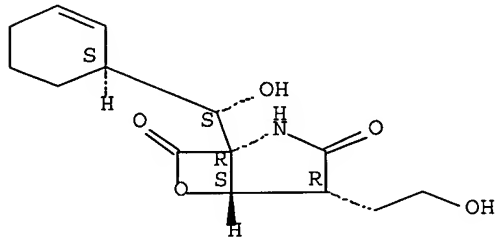
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-azidoethyl)-1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



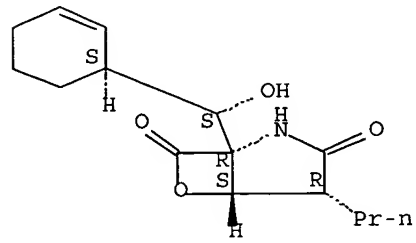
RN 855517-20-3 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-hydroxyethyl)-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



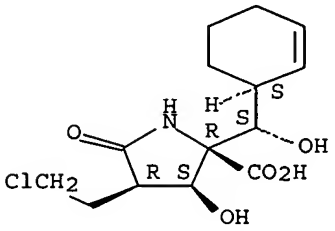
RN 855517-21-4 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-propyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 855517-11-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(structure-activity relationship studies of salinosporamide A (NPI-0052), a novel marine derived proteasome inhibitor)
RN 855517-11-2 HCAPLUS
CN D-Proline, 4-(2-chloroethyl)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

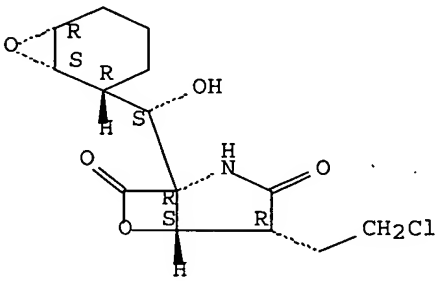


IT 855517-23-6P 855517-26-9P
RL: RCT (Reactant); SPN (Synthetic preparation);
PREP (Preparation); RACT (Reactant or reagent)
(structure-activity relationship studies of salinosporamide A (NPI-0052), a novel marine derived proteasome inhibitor)

RN 855517-23-6 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1S,2R,6R)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

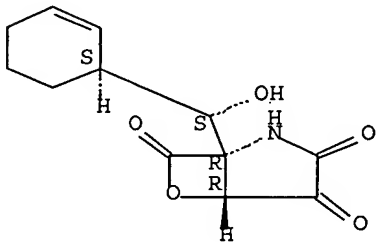
Absolute stereochemistry.



RN 855517-26-9 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,4,7-trione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-, (1R,5R)- (9CI) (CA INDEX NAME)

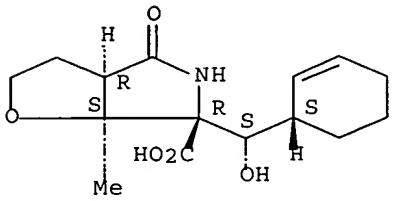
Absolute stereochemistry.



855517-12-3P 855517-24-7P 855517-25-8P
855517-27-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(structure-activity relationship studies of salinosporamide A (NPI-0052), a novel marine derived proteasome inhibitor)

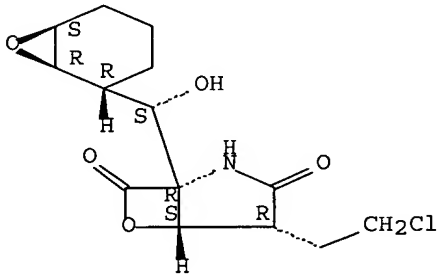
RN 855517-12-3 HCAPLUS
CN 2H-Furo[2,3-c]pyrrole-6-carboxylic acid, 6-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]hexahydro-6a-methyl-4-oxo-, (3aR,6R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



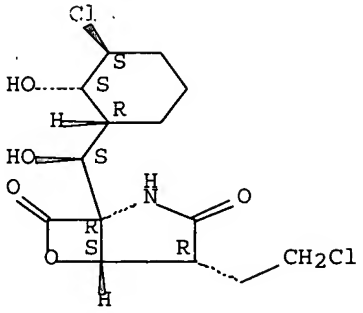
RN 855517-24-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-hydroxy(1R,2R,6S)-7-oxabicyclo[4.1.0]hept-2-ylmethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



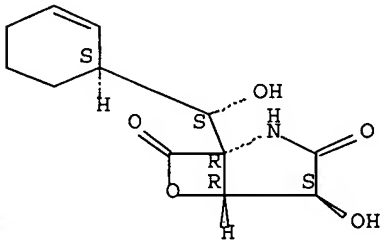
RN 855517-25-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1R,2S,3S)-3-chloro-2-hydroxycyclohexyl]hydroxymethyl]-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 855517-27-0 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hydroxy-, (1R,4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:701941 HCAPLUS Full-text
DOCUMENT NUMBER: 141:224070
TITLE: Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivatives for inhibition of proteasomes and treatment of proteasome-mediated diseases
INVENTOR(S): Stadler, Marc; Seip, Stephan; Mueller, Hartwig; Mayer-Bartschmid, Anke; Bruening, Michael-Alexander; Benet-Buchholz, Jordi; Togame, Hiroko; Dodo, Reiko; Reinemer, Peter; Bacon, Kevin; Fuchikami, Kinji; Matsukawa, Satoko; Urbahns, Klaus
PATENT ASSIGNEE(S): Bayer Healthcare AG, Germany; et al.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071382	A2	20040826	WO 2004-EP1097	20040206
WO 2004071382	A3	20050106		

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            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
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    AU 2004212296        A1    20040826    AU 2004-212296        20040206
    CA 2515940           AA    20040826    CA 2004-2515940       20040206
    EP 1597262           A2    20051123    EP 2004-708731        20040206
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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    JP 2006517934        T2    20060803    JP 2006-501755        20040206
PRIORITY APPLN. INFO.:                     EP 2003-3495       A  20030214
                                           EP 2003-7594       A  20030402
                                           WO 2004-EP1097     A  20040206

OTHER SOURCE(S):        MARPAT 141:224070
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

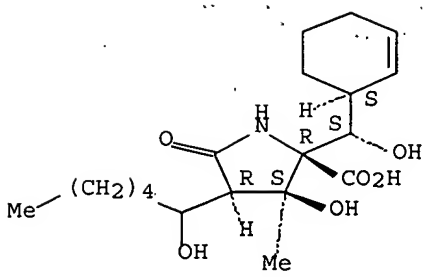
AB The title compound I and II [R1 = H, OH, methylcarbonyloxy; R2, R5 = cyclohexyl or cyclohexy-2-enyl, wherein cyclohexyl can be substituted with 0-2 hydroxy groups; R3, R6 = H or OH; R4 = H or OH; R7 = OH, cysteinyl, acetylaminoethylsulfanyl, methoxycarbonylethylsulfanyl, etc.] were prepared via fermentation of an Actinomycete of the genus Streptomyces and subsequently derivatized. Compds. I and II are useful as inhibitors of proteasomes for the treatment of proteasome-mediated diseases, such as asthma or cancer. For example, compound III was isolated from the fermentation exts. and its structure was established by HPLC-MS and multi-dimensional NMR techniques. The latter showed an IC50 =1 nM in the proteasome inhibition assay.

IT **744200-69-9P 744200-72-4P**
RL: PAC (Pharmacological activity); **PUR (Purification or recovery)**; **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; **RACT (Reactant or reagent)**; USES (Uses)
(Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)

RN 744200-69-9 HCAPLUS

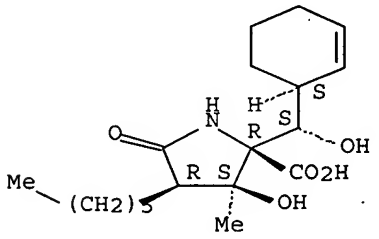
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(1-hydroxyhexyl)-3-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



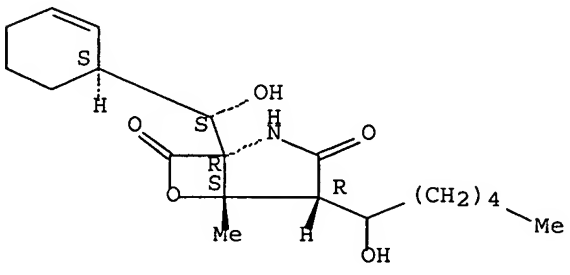
RN 744200-72-4 HCAPLUS
CN D-Proline, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



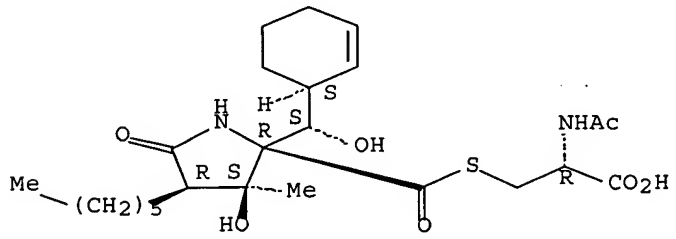
IT 744200-67-7P 744215-21-2P 744215-22-3P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide)
derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)
RN 744200-67-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(1-hydroxyhexyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



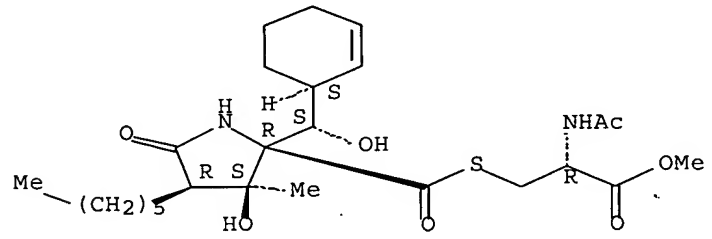
RN 744215-21-2 HCAPLUS
CN L-Cysteine, N-acetyl-, (2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



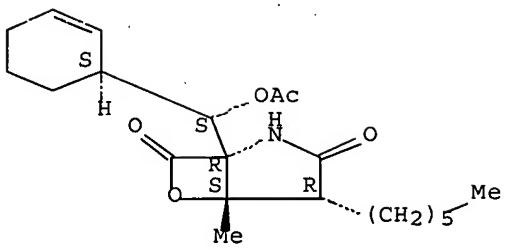
RN 744215-22-3 HCAPLUS
CN L-Cysteine, N-acetyl-, methyl ester, (2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



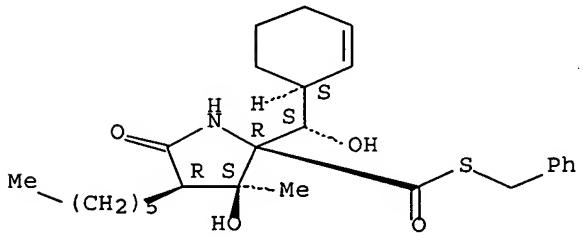
IT **744200-75-7P 744200-76-8P 744200-77-9P**
744200-78-0P 744200-79-1P 744200-80-4P
744200-81-5P 744200-82-6P 744200-83-7P
744200-84-8P
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**
; USES (Uses)
(Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide)
derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)
RN 744200-75-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(acetyloxy)(1S)-2-cyclohexen-1-ylmethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



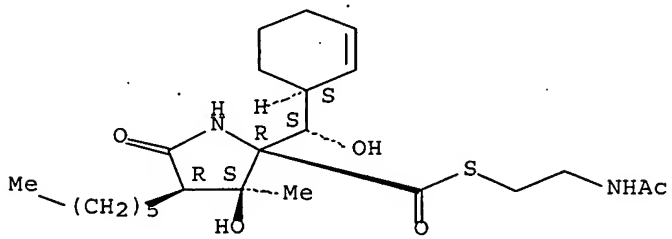
RN 744200-76-8 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, S-(phenylmethyl) ester, (2R,3S,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



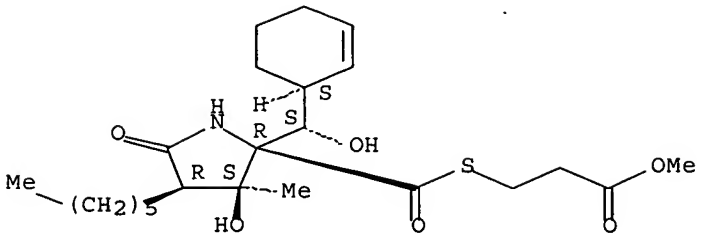
RN 744200-77-9 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, S-[2-(acetylamino)ethyl] ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



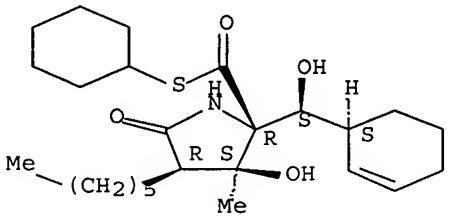
RN 744200-78-0 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



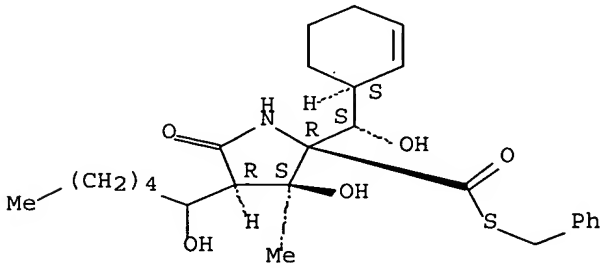
RN 744200-79-1 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, S-cyclohexyl ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



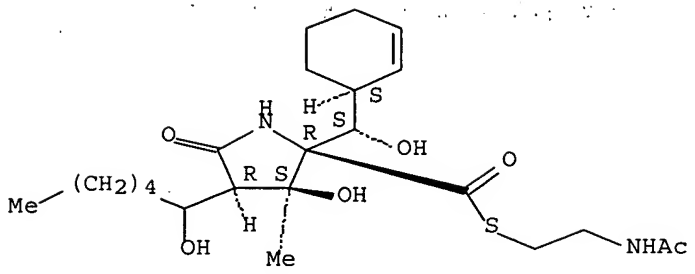
RN 744200-80-4 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(1-hydroxyhexyl)-3-methyl-5-oxo-, S-(phenylmethyl) ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



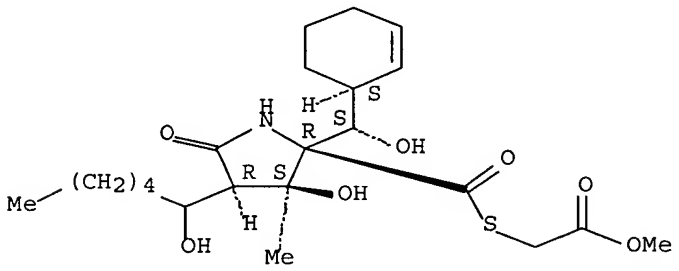
RN 744200-81-5 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(1-hydroxyhexyl)-3-methyl-5-oxo-, S-[2-(acetylamino)ethyl] ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



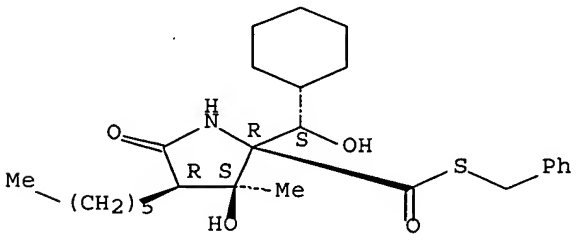
RN 744200-82-6 HCAPLUS
CN Acetic acid, [[[(2R,3S,4R)-2-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-3-hydroxy-4-(1-hydroxyhexyl)-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



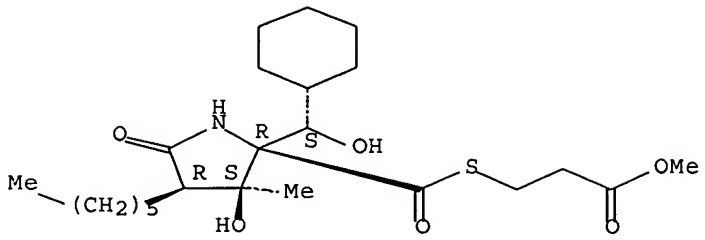
RN 744200-83-7 HCAPLUS
CN 2-Pyrrolidinecarbothioic acid, 2-[(S)-cyclohexylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-, S-(phenylmethyl) ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



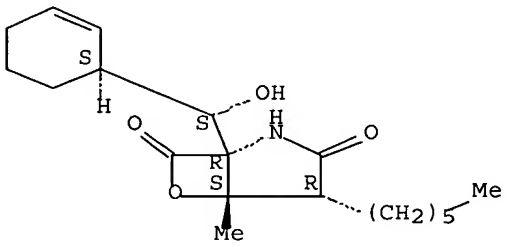
RN 744200-84-8 HCAPLUS
CN Propanoic acid, 3-[[[(2R,3S,4R)-2-[(S)-cyclohexylhydroxymethyl]-4-hexyl-3-hydroxy-3-methyl-5-oxo-2-pyrrolidinyl]carbonyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **744200-66-6P**
RL: PAC (Pharmacological activity); PRP (Properties); **PUR (Purification or recovery)**; RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(crystal structure; Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)
RN 744200-66-6 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

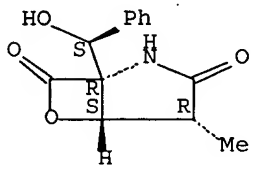


L32 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:178063 HCAPLUS Full-text
DOCUMENT NUMBER: 130:296964
TITLE: The structural requirements for inhibition of proteasome function by the lactacystin-derived β-lactone and synthetic analogs
AUTHOR(S): Corey, E. J.; Li, Wei-Dong Z.; Nagamitsu, Tohru; Fenteany, Gabriel
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Tetrahedron (1999), 55(11), 3305-3316
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of analogs of clasto-lactacystin β-lactone in which the substituents at C(5), C(7) and C(9) were systematically varied has led to a well defined structure-activity correlation for the highly selective inhibition of the mammalian 20 S proteasome.

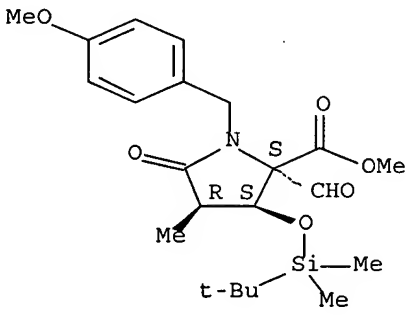
IT 223246-07-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structural requirements for inhibition of proteasome function by lactacystin-derived β-lactone and synthetic analogs)
RN 223246-07-9 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-hydroxyphenylmethyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



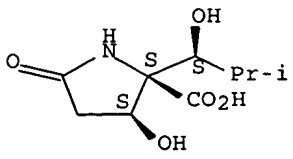
IT 212772-62-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(structural requirements for inhibition of proteasome function by lactacystin-derived β-lactone and synthetic analogs)
RN 212772-62-8 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-formyl-1-[(4-methoxyphenyl)methyl]-4-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



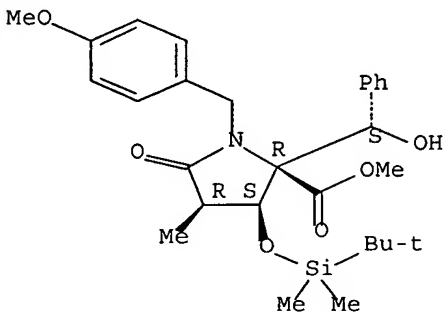
IT 212075-76-8P 223246-01-3P 223246-02-4P
223246-03-5P 223246-16-0P 223246-18-2P
223246-21-7P 223246-22-8P 223246-23-9P
223246-24-0P 223246-25-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structural requirements for inhibition of proteasome function by lactacystin-derived β-lactone and synthetic analogs)
RN 212075-76-8 HCAPLUS
CN D-Proline, 3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



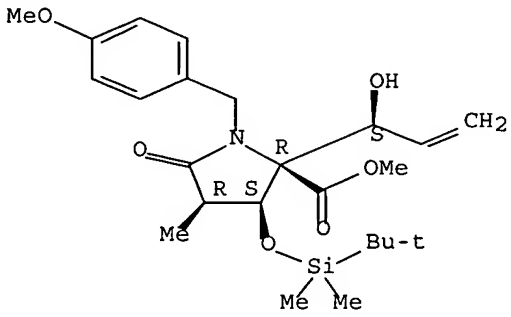
RN 223246-01-3 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-[(S)-hydroxyphenylmethyl]-1-[(4-methoxyphenyl)methyl]-4-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



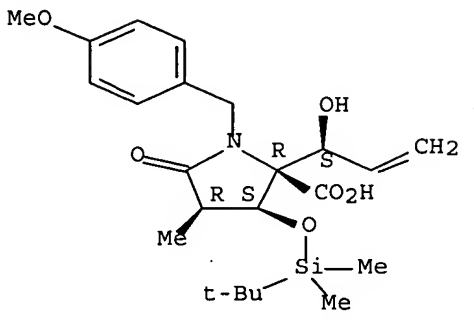
RN 223246-02-4 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-[(1S)-1-hydroxy-2-propenyl]-1-[(4-methoxyphenyl)methyl]-4-methyl-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



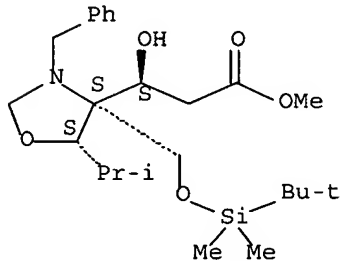
RN 223246-03-5 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-[(1S)-1-hydroxy-2-propenyl]-1-[(4-methoxyphenyl)methyl]-4-methyl-5-oxo-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



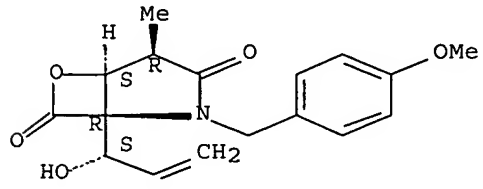
RN 223246-16-0 HCAPLUS
CN 4-Oxazolidinepropanoic acid, 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-β-hydroxy-5-(1-methylethyl)-3-(phenylmethyl)-, methyl ester, (βS,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



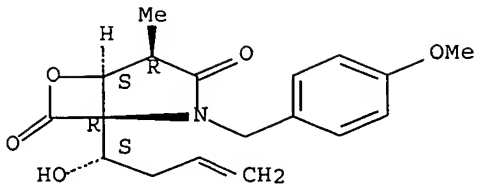
RN 223246-18-2 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(1S)-1-hydroxy-2-propenyl]-2-[(4-methoxyphenyl)methyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



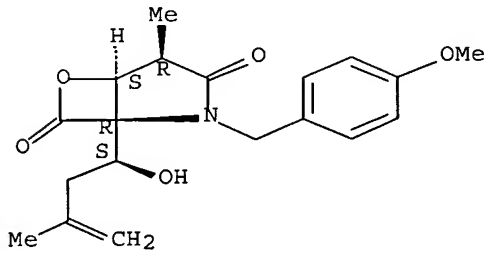
RN 223246-21-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(1S)-1-hydroxy-3-butenyl]-2-[(4-methoxyphenyl)methyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



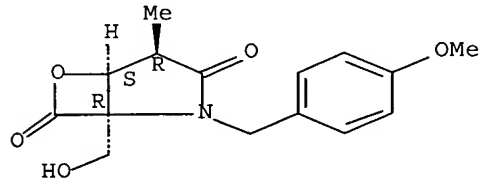
RN 223246-22-8 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(1S)-1-hydroxy-3-methyl-3-butenyl]-2-[(4-methoxyphenyl)methyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



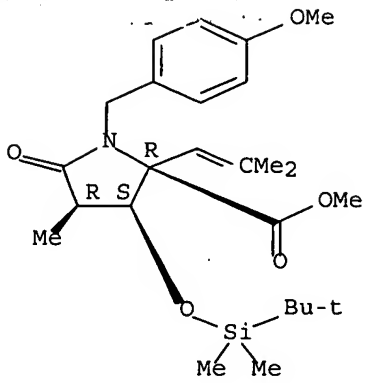
RN 223246-23-9 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-(hydroxymethyl)-2-[(4-methoxyphenyl)methyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



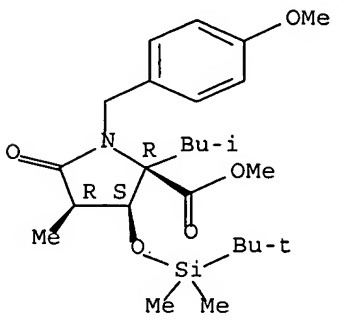
RN 223246-24-0 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-4-methyl-2-(2-methyl-1-propenyl)-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 223246-25-1 HCAPLUS
CN D-Proline, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[(4-methoxyphenyl)methyl]-4-methyl-2-(2-methylpropyl)-5-oxo-, methyl ester, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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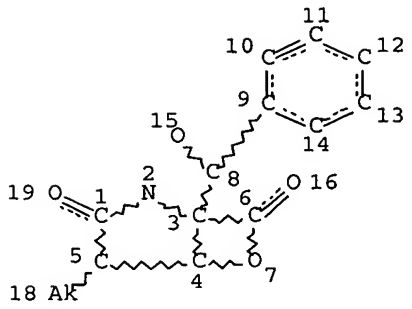
L4 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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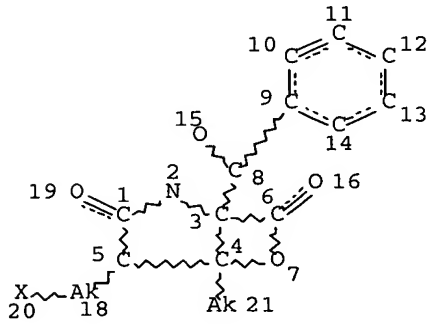
L7 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)PREP+NT/RL
L8 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
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L15           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND (C6 AND NCOC2)/ES
              AND O>3
L16           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15(L)RACT+NT/RL AND L15(L)PRE
              P+NT/RL
L17         123 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6/ES AND O>4 AND L12
L18          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17(L)RACT+NT/RL AND L17(L)PRE
              P+NT/RL
L19         144 SEA FILE=REGISTRY ABB=ON  PLU=ON  O>4 AND N>0 AND L12
L20         119 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19(L)RACT+NT/RL AND L19(L)PRE
              P+NT/RL
L22          30 SEA FILE=REGISTRY ABB=ON  PLU=ON  SI/ELS AND L12
L23           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22(L)RACT+NT/RL AND L22(L)PRE
              P+NT/RL
L24           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND ZN/ELS
L25           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24(L)RACT+NT/RL
L27     1537291 SEA FILE=REGISTRY ABB=ON  PLU=ON  NC4/ES
L28          69 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND L27
L29          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28(L)RACT+NT/RL AND L28(L)PRE
              P+NT/RL
L30          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (L14 OR L16 OR L18 OR
              L20 OR L23 OR L25 OR L29)
L31           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L11
L33           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT (L30 OR L31)


=> d l33 ibib abs hitstr 1-4

L33  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:567385  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:244731
TITLE:                    New cytotoxic salinosporamides from the marine
                          actinomycete Salinispora tropica
```
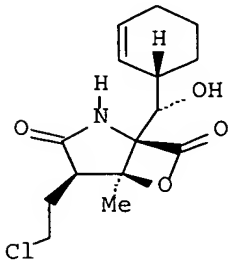

AUTHOR(S): Williams, Philip G.; Buchanan, Greg O.; Feling, Robert H.; Kauffman, Christopher A.; Jensen, Paul R.; Fenical, William
CORPORATE SOURCE: Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California-San Diego, La Jolla, CA, 92093-0204, USA
SOURCE: Journal of Organic Chemistry (2005), 70(16), 6196-6203
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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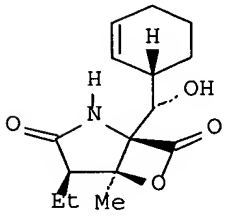
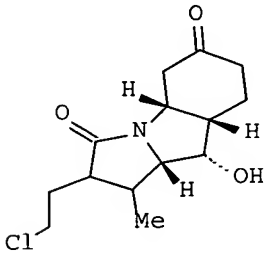


II



III

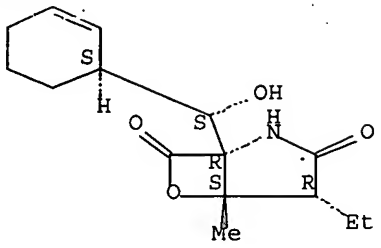
AB An extensive study of the secondary metabolites produced by the obligate marine actinomycete S. tropica (strain CNB-392), the producing microbe of the potent proteasome inhibitor salinosporamide A (I), has led to the isolation of 7 related γ-lactams. The most important of these compds. were salinosporamide B (II), which is the deschloro analog of I, and salinosporamide C (III), which is a decarboxylated pyrrole analog. New SAR data for all 8 compds., derived from extensive testing against the human colon carcinoma HCT-116 and the 60-cell-line panel at the NCI, indicate that the chloroethyl moiety plays a major role in the enhanced activity of I.

IT **863126-95-8P**, Salinosporamide B
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); **PUR (Purification or recovery)**; BIOL (Biological study); OCCU (Occurrence); **PREP (Preparation)**
(new cytotoxic salinosporamides from the marine actinomycete Salinispora tropica)

RN 863126-95-8 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-ethyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:29196 HCAPLUS Full-text
DOCUMENT NUMBER: 142:107451
TITLE: Methods using [3.2.0]-heterocyclic compounds and analogs thereof for the treatment of cancer, an inflammatory condition, and/or an infectious disease
INVENTOR(S): Palladino, Michael; Neuteboom, Saskia Theodora Cornelia; Macherla, Venkata Rami Reddy; Potts, Barbara Christine
PATENT ASSIGNEE(S): Nereus Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005002572	A2	20050113	WO 2004-US19543		20040618
WO 2005002572	A3	20050512			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004253478	A1	20050113	AU 2004-253478		20040618
CA 2532066	AA	20050113	CA 2004-2532066		20040618
US 2005049294	A1	20050303	US 2004-871368		20040618
EP 1638552	A2	20060329	EP 2004-776757		20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004011677	A	20060829	BR 2004-11677		20040618
PRIORITY APPLN. INFO.:			US 2003-480270P	P	20030620
			US 2004-566952P	P	20040430
			WO 2004-US19543	W	20040618

OTHER SOURCE(S): MARPAT 142:107451

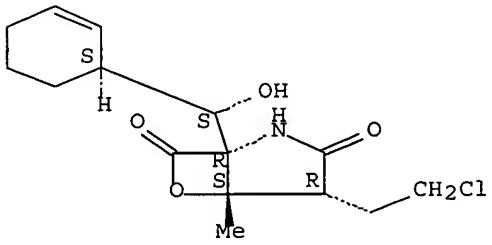
AB Methods are disclosed for treating cancer, inflammatory conditions, and/or infectious disease in an animal comprising administering a therapeutically effective amount of a heterocyclic compound The animal is a mammal, preferably a human or a rodent. Production of compds. by fermentation and synthesis is described.

IT **437742-34-2P**, Salinosporamide A
RL: **BPN (Biosynthetic preparation)**; DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); **PUR (Purification or recovery)**; RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(heterocyclic compds. and analogs for treatment of cancer, inflammation, and/or infectious disease)

RN 437742-34-2 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

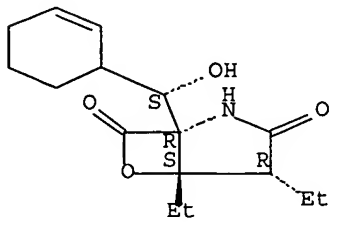


IT **823229-30-7P 823229-32-9P**
RL: **BPN (Biosynthetic preparation)**; PAC (Pharmacological activity); **PUR (Purification or recovery)**; RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(heterocyclic compds. and analogs for treatment of cancer, inflammation, and/or infectious disease)

RN 823229-30-7 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-diethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

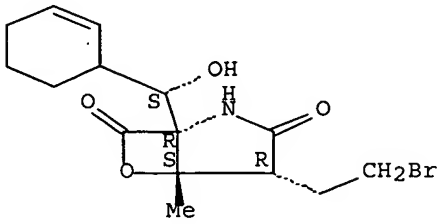


RN 823229-32-9 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-bromoethyl)-1-[(S)-2-

cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

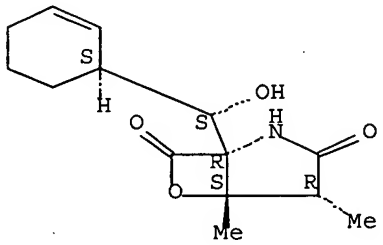


IT 823229-26-1P 823229-28-3P
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic compds. and analogs for treatment of cancer, inflammation, and/or infectious disease)

RN 823229-26-1 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4,5-dimethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

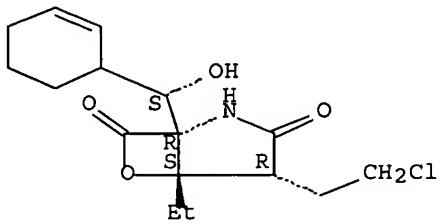
Absolute stereochemistry.



RN 823229-28-3 HCAPLUS

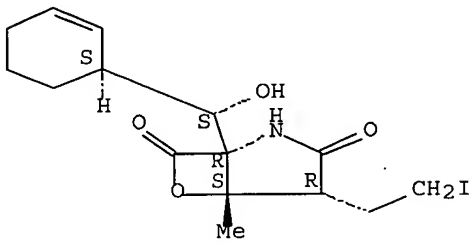
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-2-cyclohexen-1-ylhydroxymethyl]-5-ethyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



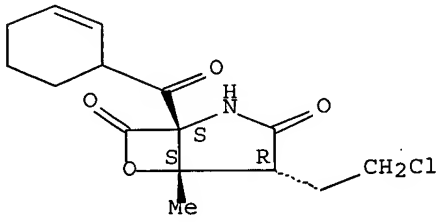
IT 823229-34-1P 823229-43-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(heterocyclic compds. and analogs for treatment of cancer, inflammation, and/or infectious disease)
RN 823229-34-1 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-iodoethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



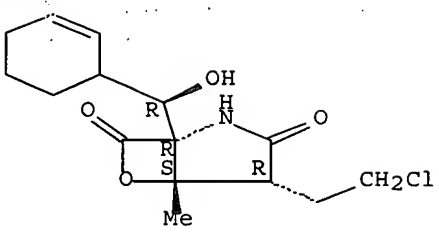
RN 823229-48-7 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-(2-cyclohexen-1-ylcarbonyl)-5-methyl-, (1S,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



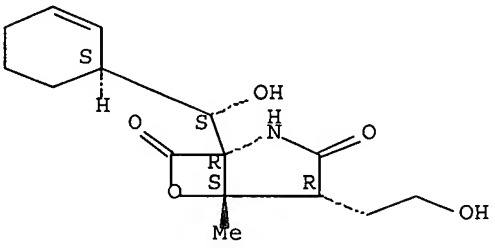
IT 823229-52-3P 823229-54-5P 823229-56-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic compds. and analogs for treatment of cancer, inflammation, and/or infectious disease)
RN 823229-52-3 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(R)-2-cyclohexen-1-ylhydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 823229-54-5 HCAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(2-hydroxyethyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 823229-56-7 HCAPLUS
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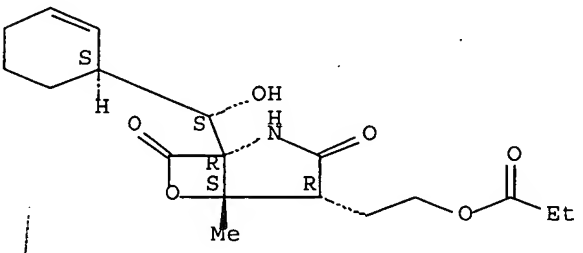
Absolute stereochemistry.



L33 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1127086 HCAPLUS Full-text
DOCUMENT NUMBER: 142:54864
TITLE: Salinosporamides and methods for use thereof
INVENTOR(S): Fenical, William; Jensen, Paul; Mincer, Tracy; Feling, Robert H. R.
PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: U.S. Pat. Appl. Publ., 30 pp., Cont-in-part of U.S. Ser. No. 600,854.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004259856	A1	20041223	US 2004-838157	20040430
US 2004138196	A1	20040715	US 2003-600854	20030620
AU 2004253879	A1	20050113	AU 2004-253879	20040618
CA 2530215	AA	20050113	CA 2004-2530215	20040618
WO 2005003137	A1	20050113	WO 2004-US19453	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638977	A1	20060329	EP 2004-776728	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1823070	A	20060823	CN 2004-80020530	20040618
US 2005239866	A1	20051027	US 2005-147622	20050607

PRIORITY APPLN. INFO.:

US 2002-391314P	P	20020624
US 2003-600854	A2	20030620
US 2004-838157	A	20040430
WO 2004-US19453	W	20040618

OTHER SOURCE(S): MARPAT 142:54864

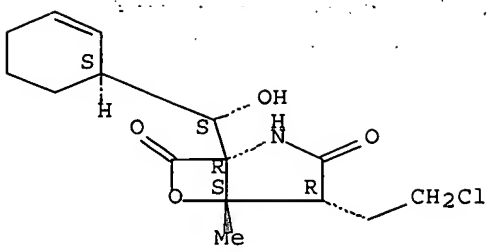
AB The present invention is based on the discovery that certain fermentation products of the marine actinomycete strains CNB392 and CNB476 are effective inhibitors of hyperproliferative mammalian cells. The CNB392 and CNB476 strains lie within the family Micromonosporaceae, and the generic epithet Salinospora has been proposed for this obligate marine group. The reaction products produced by this strain are classified as salinosporamides, and are particularly advantageous in treating neoplastic disorders due to their low mol. weight, low IC 50 values, high pharmaceutical potency, and selectivity for cancer cells over fungi.

IT **437742-34-2P**, Salinosporamide A
RL: **BMF (Bioindustrial manufacture)**; **BPN (Biosynthetic preparation)**; BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(anticancer salinosporamide)

RN 437742-34-2 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L33 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:570502 HCAPLUS Full-text
DOCUMENT NUMBER: 141:105361
TITLE: Salinosporamides and methods for use thereof
INVENTOR(S): Fenical, William; Jensen, Paul; Mincer, Tracy; Feling, Robert H. R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20041381 96	A1	20040715	US 2003-600854	20030620
US 2004259856	A1	20041223	US 2004-838157	20040430
AU 2004253879	A1	20050113	AU 2004-253879	20040618
CA 2530215	AA	20050113	CA 2004-2530215	20040618
WO 2005003137	A1	20050113	WO 2004-US19453	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638977	A1	20060329	EP 2004-776728	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1823070	A	20060823	CN 2004-80020530	20040618
US 2005239866	A1	20051027	US 2005-147622	20050607

PRIORITY APPLN. INFO.:	US 2002-391314P	P	20020624
	US 2003-600854	A2	20030620
	US 2004-838157	A	20040430
	WO 2004-US19453	W	20040618

OTHER SOURCE(S): MARPAT 141:105361

AB The present invention is based on the discovery that certain fermentation products of the marine actinomycete strains CNB392 and CNB476 are effective inhibitors of hyperproliferative mammalian cells. The CNB392 and CNB476 strains lie within the family Micromonosporaceae, and the generic epithet

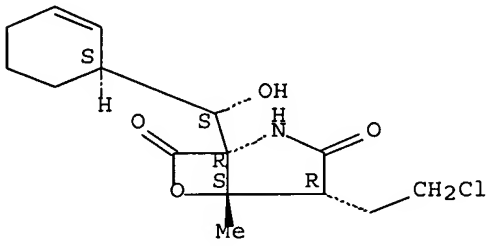
Salinospora has been proposed for this obligate marine group. The reaction products produced by this strain are classified as salinosporamides, and are particularly advantageous in treating neoplastic disorders due to their low mol. weight, low IC 50 values, high pharmaceutical potency, and selectivity for cancer cells over fungi.

IT **437742-34-2P**, Salinosporamide A
RL: BSU (Biological study, unclassified); PRP (Properties); **PUR (Purification or recovery)**; BIOL (Biological study); **PREP (Preparation)**
(salinosporamides and anticancer use thereof)

RN 437742-34-2 HCAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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licensed to Beilstein GmbH and MDL Information Systems GmbH

FILE LAST UPDATED ON JUNE 16, 2006

FILE COVERS 1771 TO 2006.
*** FILE CONTAINS  9,606,495 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
   separate documents and can not be searched together in one query.
   Reaction data for BEILSTEIN compounds may be displayed
   immediately with the display codes PRE (preparations) and REA
   (reactions).  A substance answer set retrieved after the search
   for a chemical name, a compounds with available reaction
   information by combining with PRE/FA, REA/FA or more generally
   with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
   between a BEILSTEIN compound and belonging reactions. For mo
   detailed reaction searches BRNs can be searched as reaction
   partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

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* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE    *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE           *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                         *
* FOR PRICE INFORMATION SEE HELP COST                                 *
**********************************************************************
    NEW
* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE
  SEARCHED, SELECTED AND TRANSFERRED.
* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES,
  ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A
  COMPOUND AT A GLANCE.

=> d que l35
L35           5 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  (10187632/RX.PBRN OR
                10190531/RX.PBRN OR 10190532/RX.PBRN OR 10190534/RX.PBRN OR
                10193505/RX.PBRN OR 10193538/RX.PBRN OR 9349224/RX.PBRN)


=> d l35 ide rx 1-5


L35  ANSWER 1 OF 5 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN
   This is a Reaction Document. Display Formats IDE and FA are not available
   here.

Reaction:
RX
     Reaction ID (.ID):              10072318
     Reactant BRN (.RBRN):           9349224
     Reactant (.RCT):                salinosporamide A
     Product BRN (.PBRN):            10193538
     Product (.PRO):                 NPI-2070
     No. of React. Details (.NVAR):  1
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Reaction Details:
RX

Reaction RID (.RID):	10072318.1
Reaction Classification (.CL):	Preparation
Yield (.YDT):	11 percent (BRN=10193538)
Reagent (.RGT):	NaI
Solvent (.SOL):	acetone
Time (.TIM):	6 day(s)

Reference(s):
1. Macherla, Venkat R.; Mitchell, Scott S.; Manam, Rama Rao; Reed, Katherine A.; Chao, Ta-Hsiang; Nicholson, Benjamin; Deyanat-Yazdi, Gordafaried; Mai, Bao; Jensen, Paul R.; Fenical, William F.; Neuteboom, Saskia T. C.; et al., J. Med. Chem., CODEN: JMCMAR, SIR48(11), <2005>, 3684 - 3687; BABS-6528037

L35 ANSWER 2 OF 5 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN
This is a Reaction Document. Display Formats IDE and FA are not available here.

Reaction:
RX

Reaction ID (.ID):	10072315
Reactant BRN (.RBRN):	9349224
Reactant (.RCT):	salinosporamide A
Product BRN (.PBRN):	10187632
Product (.PRO):	NPI-2062
No. of React. Details (.NVAR):	1

Reaction Details:
RX

Reaction RID (.RID):	10072315.1
Reaction Classification (.CL):	Preparation
Reagent (.RGT):	Dess-Martin periodinane
Solvent (.SOL):	CH2Cl2
Time (.TIM):	2 hour(s)
Temperature (.T):	20 Cel

Reference(s):
1. Macherla, Venkat R.; Mitchell, Scott S.; Manam, Rama Rao; Reed, Katherine A.; Chao, Ta-Hsiang; Nicholson, Benjamin; Deyanat-Yazdi, Gordafaried; Mai, Bao; Jensen, Paul R.; Fenical, William F.; Neuteboom, Saskia T. C.; et al., J. Med. Chem., CODEN: JMCMAR, SIR48(11), <2005>, 3684 - 3687; BABS-6528037

L35 ANSWER 3 OF 5 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN
This is a Reaction Document. Display Formats IDE and FA are not available here.

Reaction:
RX

Reaction ID (.ID):	10001896
Reactant BRN (.RBRN):	10187632
Reactant (.RCT):	NPI-2062
Product BRN (.PBRN):	10190531
Product (.PRO):	NPI-2076
No. of React. Details (.NVAR):	1

Reaction Details:
RX

Reaction RID (.RID): 10001896:1
Reaction Classification (.CL): Preparation
Yield (.YDT): 30 percent (BRN=10190531)
Reagent (.RGT): NaBH4
Solvent (.SOL): 1,2-dimethoxy-ethane, H2O
Time (.TIM): 14 min
Temperature (.T): -78 Cel
Reference(s):
1. Macherla, Venkat R.; Mitchell, Scott S.; Manam, Rama Rao; Reed, Katherine A.; Chao, Ta-Hsiang; Nicholson, Benjamin; Deyanat-Yazdi, Gordafaried; Mai, Bao; Jensen, Paul R.; Fenical, William F.; Neuteboom, Saskia T. C.; et al., J. Med. Chem., CODEN: JMCMAR, SIR48(11), <2005>, 3684 - 3687; BABS-6528037

L35 ANSWER 4 OF 5 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN
This is a Reaction Document. Display Formats IDE and FA are not available here.

Reaction:
RX
Reaction ID (.ID): 9918214
Reactant BRN (.RBRN): 10102697
Reactant (.RCT): 1-(cyclohex-2-enyl-hydroxy-methyl)-4-(2-hydroxy-ethyl)-5-methyl-6-oxa-2-aza-bicyclo<3.2.0>heptane-3,7-dione
Product BRN (.PBRN): 9349224
Product (.PRO): salinosporamide A
No. of React. Details (.NVAR): 1

Reaction Details:
RX
Reaction RID (.RID): 9918214.1
Reaction Classification (.CL): Preparation
Yield (.YDT): 6.8 mg (BRN=9349224)
Reagent (.RGT): PH3PCl2
Solvent (.SOL): pyridine, acetonitrile
Time (.TIM): 4 hour(s)
Temperature (.T): 20 Cel
Reference(s):
1. Endo, Atsushi; Danishefsky, Samuel J., J. Am. Chem. Soc., CODEN: JACSAT, SIR127(23), <2005>, 8298 - 8299; BABS-6510529

L35 ANSWER 5 OF 5 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN
This is a Reaction Document. Display Formats IDE and FA are not available here.

Reaction:
RX
Reaction ID (.ID): 9623610
Reactant BRN (.RBRN): 9727083
Reactant (.RCT): 2-(cyclohex-2-enyl-hydroxy-methyl)-3-hydroxy-4-(2-hydroxy-ethyl)-3-methyl-5-oxo-pyrrolidine-2-carboxylic acid
Product BRN (.PBRN): 9349224
Product (.PRO): salinosporamide A
No. of React. Details (.NVAR): 1

Reaction Details:

Reaction RID (.RID): 9623610.1
Reaction Classification (.CL): Multistage
Yield (.YDT): 100 mg (BRN=9349224)
Nr. of Stages (.SNR): 2
Stage 1
Reagent (.RGT): bis(2-oxo-3-oxazolidinyl)phosphonic chloride, pyridine
Solvent (.SOL): CH2Cl2
Time (.TIM): 1 hour(s)
Temperature (.T): 23 Cel
Stage 2
Reagent (.RGT): pyridine, PPh3Cl2
Solvent (.SOL): acetonitrile, CH2Cl2
Time (.TIM): 1 hour(s)
Temperature (.T): 23 Cel
Reference(s):
1. Reddy, Leleti Rajender; Saravanan, P.; Corey, E. J., J. Am. Chem. Soc., CODEN: JACSAT, 126(20), <2004>, 6230 - 6231; BABS-6446758

INVENTOR SEARCH

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=> d que l42
L38        2176 SEA ("COREY E"/AU OR "COREY E J"/AU OR "COREY E J AND GREGORY
                A REICHARD"/AU OR "COREY E JAMES"/AU) OR ("COREY ELIAS J"/AU
                OR "COREY ELIAS J JR"/AU OR "COREY ELIAS JAMES"/AU)
L39          16 SEA L38 AND ?SALINO?
L40          15 SEA L38 AND ?SPORAMID?
L41          16 SEA L39 OR L40
L42           7 DUP REM L41 (9 DUPLICATES REMOVED)


=> d l42 ibib abs 1-7

L42  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:1117942  HCAPLUS  Full-text
DOCUMENT NUMBER:          144:22739
TITLE:                    Proteasome Inhibition by a Totally Synthetic
                          β-Lactam Related to Salinosporamide A
                          and Omuralide
AUTHOR(S):                Hogan, Philip C.; Corey, E. J.
CORPORATE SOURCE:         Department of Chemistry and Chemical Biology, Harvard
                          University, Cambridge, MA, 02138, USA
SOURCE:                   Journal of the American Chemical Society (2005),
                          127(44), 15386-15387
                          CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
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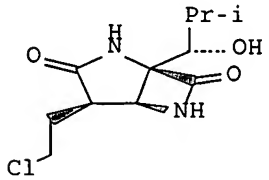

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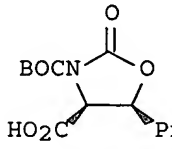

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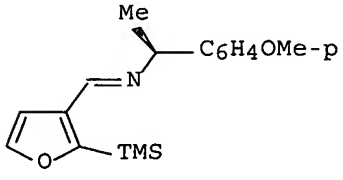

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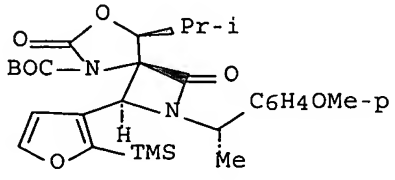

IV

AB A new and effective proteasome inhibitor, β-lactam I, has been accessed enantioselectively by multistep synthesis from the readily prepared intermediates II and III which were joined by a [2 + 2]-cycloaddn. reaction to form the spiro β-lactam IV stereoselectively. The intermediate IV was converted to I in seven steps and 30% overall yield. The β-lactam I is stable for many days in water at pH 7, in contrast to the natural β-lactones **salinosporamide** A and omuralide. In common with **salinosporamide** A and omuralide, the β-lactam I effectively inhibits the mammalian proteasome.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2005:470433 HCAPLUS Full-text
DOCUMENT NUMBER: 143:172666
TITLE: An Efficient, Stereocontrolled Synthesis of a Potent Omuralide-**Salinosporin** Hybrid for Selective Proteasome Inhibition
AUTHOR(S): Reddy, Leleti Rajender; Fournier, Jean-Francois; Reddy, B. V. Subba; **Corey, E. J.**
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (2005), 127(25), 8974-8976
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:172666
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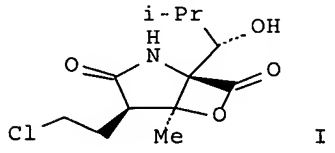

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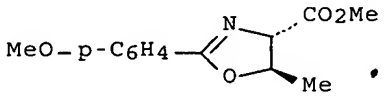


II

AB A short and highly stereocontrolled synthesis of the potent proteasome inhibitor I (antiprotealide) from the (S)-threonine-derived oxazoline II has been developed. The key steps include a diastereoselective aldol coupling, an internal carbo-titanation using Kulinkovich reagent, diastereoselective cyclization, and demethylation with [Me2AlTeMe]2. The potency of I against the β5-subunit of human 20S proteasome was about 2.5 times that of omuralide.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

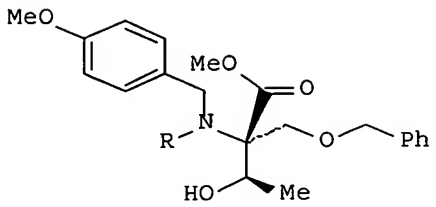
L42 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2005:443900 HCAPLUS Full-text
DOCUMENT NUMBER: 143:115371
TITLE: New Synthetic Route for the Enantioselective Total Synthesis of **Salinosporamide** A and

Biologically Active Analogues
AUTHOR(S): Reddy, Leleti Rajender; Fournier, Jean-Francois; Reddy, B. V. Subba; **Corey, E. J.**
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Organic Letters (2005), 7(13), 2699-2701
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:115371
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A total synthesis of the **salinosporamide** analog I is described. A key step early in the synthesis was the Baylis-Hillman cyclization of II to the γ-lactam III with 9:1 diastereoselectivity and in good yield. In addition, the γ-lactam III has been transformed efficiently into β-Me omuralide (IV).
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:340603 HCAPLUS Full-text
DOCUMENT NUMBER: 141:54117
TITLE: A Simple Stereocontrolled Synthesis of **Salinosporamide** A
AUTHOR(S): Reddy, Leleti Rajender; Saravanan, P.; **Corey, E. J.**
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (2004), 126(20), 6230-6231
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:54117
GI



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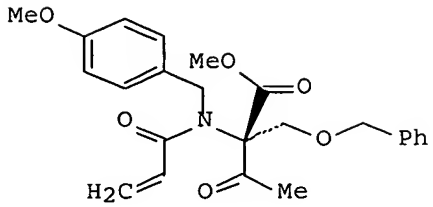
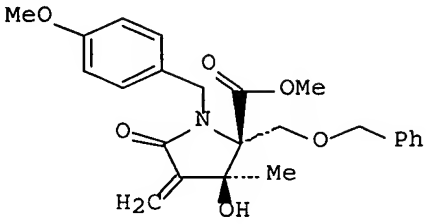


II

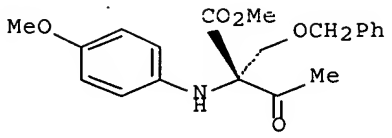


III

AB A simple and effective stereocontrolled synthesis of **salinosporamide** A has been developed. Of special note is the direct conversion of amino(benzyloxymethyl)hydroxybutanoate I (R = H) to acryloyl derivative I (R = COCH:CH2). Also, quinuclidine proved to be superior to other bases in the cyclization of oxybutanoate II to oxopyrrolidinecarboxylate III. This process, the first synthesis of **salinosporamide** A, is capable of providing the compound in substantial quantities for further biol. studies. **Salinosporamide** A was of special interest as a synthetic target because of its potent in vitro cytotoxic activity against many tumor cell lines (IC50 values of 10 nM or less).

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:274086 HCAPLUS Full-text
DOCUMENT NUMBER: 145:7903
TITLE: Novel Bicyclization Reaction Leading to a Fused β-Lactone
AUTHOR(S): Reddy, Leleti Rajender; **Corey, E. J.**
CORPORATE SOURCE: Harvard University, Cambridge, MA, 02138, USA
SOURCE: Organic Letters (2006), 8(8), 1717-1719
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The reaction of acryloyl chloride with the amino ketone I in the presence of pyridine produces bicyclic β-lactones rather than the corresponding acrylamide, which can be the major product under other conditions and which is an intermediate for the synthesis of **salinosporamide** A.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1154365 HCAPLUS Full-text
DOCUMENT NUMBER: 143:422201
TITLE: Preparation of **salinosporamide** A for use in anticancer pharmaceutical compositions as proteasome inhibitors
INVENTOR(S): **Corey, Elias J.**
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005099687	A2	20051027	WO 2005-US12113	20050411
WO 2005099687	A3	20051229		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-560877P P 20040409
OTHER SOURCE(S): MARPAT 143:422201
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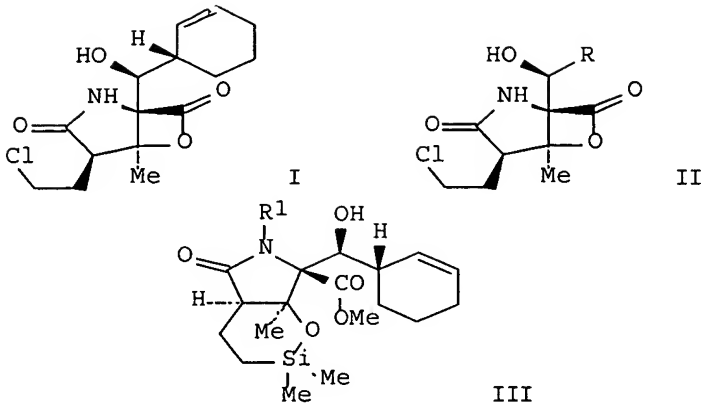

I II III

AB **Salinosporamide** A (I) and its analogs, such as II (R = alkyl, alkenyl, etc.), were enantioselectively synthesized starting from N-(4-methoxybenzoyl)-L-threonine Me ester via several novel synthetic intermediates, such as lactam II (R1 = CH2C6H4-4-OMe). The compds. of this invention have been shown to inhibit the proteasome, an intracellular enzyme complex that destroys proteins the cell no longer needs. Without the proteasome, proteins would build up and clog cellular machinery. Fast-growing cancer cells make especially heavy use of the proteasome, so thwarting its action is a compelling drug strategy.

L42 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1106831 HCAPLUS Full-text
DOCUMENT NUMBER: 143:386848
TITLE: Simple stereocontrolled synthesis of **salinosporamide** A
INVENTOR(S): **Corey, Elias J.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005228186	A1	20051013	US 2004-821621	20040409
WO 2005113558	A2	20051201	WO 2005-US12218	20050411
WO 2005113558	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-821621 A 20040409
OTHER SOURCE(S): CASREACT 143:386848

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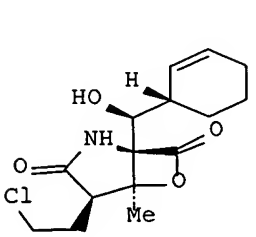
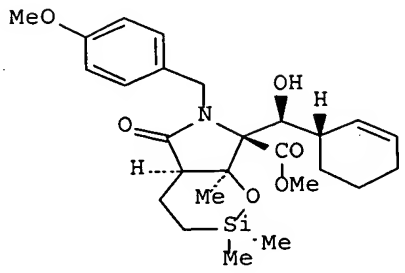


I



II

AB A simple and effective stereocontrolled synthesis of (-)- **salinosporamide** A (I) was disclosed. The process, the first total synthesis of **salinosporamide** A, is capable of providing the compound in substantial quantities for further biol. studies. The disclosed synthetic scheme started from N-(4-methoxybenzoyl)-L-threonine Me ester and included the preparation of several novel synthetic intermediate compds., such as lactam II. **Salinosporamide** A is a synthetic target of special interest because it has previously shown proteasome inhibiting activity and shown cytotoxic activity in vitro against many tumor cell lines (IC50 values of 10 nM or less).